As confidentially submitted to the Securities and Exchange Commission on April 4, 2022.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

FRACTYL HEALTH, INC.
(Exact name of registrant as specified in its charter)

Delaware	**3841**	**27-3553477**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

17 Hartwell Avenue
Lexington, MA 02421
Telephone: (781) 902-8800
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Harith Rajagopalan, M.D., Ph.D.
Chief Executive Officer
Fractyl Health, Inc.
17 Hartwell Avenue
Lexington, MA 02421
(781) 902-8800
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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New York, New York 10020	**New York, New York 10018**
(212) 906-1200	**(212) 813-8800**

Approximate date of commencement of proposed sale to the public:
As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	**Accelerated filer**	☐
Non-accelerated filer	☒	**Smaller reporting company**	☒
		Emerging growth company	☒

If an emerging growth company, indicate by checkmark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided to Section 7(a)(2)(B) of the Securities Act. ☐

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus dated , 2022.

P R O S P E C T U S

Shares

Common Stock

This is Fractyl Health, Inc.'s initial public offering. We are selling shares of our common stock.

We expect the initial public offering price to be between $ and $ per share. Currently, no public market exists for our common stock. After the pricing of the offering, we expect that our common stock will trade on the Nasdaq Global Market under the symbol "GUTS."

We are an "emerging growth company" and a "smaller reporting company" under the federal securities laws and are subject to reduced public company disclosure standards. See "Prospectus Summary—Implications of Being an Emerging Growth Company and a Smaller Reporting Company."

Investing in our common stock involves risks. See "Risk Factors" beginning on page 16 of this prospectus.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We refer you to "Underwriting" beginning on page 223 for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about , 2022.

BofA Securities **Morgan Stanley** **Evercore ISI**

The date of this prospectus is , 2022

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus, any amendment or supplement to this prospectus, or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

BASIS OF PRESENTATION

Except where the context otherwise requires or where otherwise indicated, the terms "Fractyl," "Fractyl Health," "we," "us," "our," "our company," "Company" and "our business" refer to Fractyl Health, Inc and its subsidiary.

The consolidated financial statements include the accounts of Fractyl Health, Inc. Our financial statements have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. Our fiscal year ends on December 31 of each year. References to 2021 refer to the year ended December 31, 2021. Our most recent fiscal year ended on December 31, 2021.

Certain monetary amounts, percentages and other figures included in this prospectus have been subject to rounding adjustments. Percentage amounts included in this prospectus have not in all cases been calculated on the basis of such rounded figures, but on the basis of such amounts prior to rounding. For this reason, percentage amounts in this prospectus may vary from those obtained by performing the same calculations using the figures in our consolidated financial statements included elsewhere in this prospectus. Certain other amounts that appear in this prospectus may not sum due to rounding.

TRADEMARKS AND TRADENAMES

This prospectus includes our trademarks and trade names, including, without limitation, REVITA, REJUVA and our logo, which are our property and are protected under applicable intellectual property laws. This prospectus also contains trademarks, trade names and service marks of other companies, which are the property of their respective owners. Solely for convenience, trademarks, trade names and service marks referred to in this prospectus may appear without the ®, ™ or SM symbols, but such references are not intended to indicate, in any way, that we or the applicable owner will not assert, to the fullest extent permitted under applicable law, our or its rights or the right of any applicable licensor to these trademarks, trade names and service marks. We do not intend our use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

INDUSTRY AND OTHER DATA

This prospectus contains industry, market and competitive position data from our own internal estimates and research as well as industry and general publications and research surveys and studies conducted by independent third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believe to be reliable. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management's understanding of industry conditions. Management is responsible for the accuracy of our internal company research and believes such information is reliable and the market definitions are appropriate. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in "Risk Factors". These and other factors could cause results to differ materially from these expressed in the estimates made by the independent third parties and by us.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read the entire prospectus carefully, including "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus, before making an investment decision. Some of the statements in this prospectus constitute forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements."

Overview

We are an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes, or T2D. Despite advances in treatment over the last 50 years, metabolic diseases in general, and T2D in particular, continue to be a principal and rapidly growing driver of morbidity and mortality in the 21st century. The International Diabetes Federation estimates that nearly 600 million people are expected to be living with T2D globally by 2035. In the United States alone, the Centers for Disease Control and Prevention estimates that nearly 27 million people have been diagnosed with T2D. A study published in the New England Journal of Medicine in 2021 reported that glycemic control is worsening in this population and approximately half of these individuals are not achieving targeted disease control despite the availability of over 60 approved drugs for the condition. Our goal is to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. The Revita DMR System, or Revita, our lead product candidate, is designed to remodel the duodenal lining via hydrothermal ablation in order to edit abnormal intestinal nutrient sensing and signaling mechanisms that we believe are a root cause of metabolic diseases. Led by our ongoing Revitalize-1 pivotal study, we have initiated a broad clinical program, Revitalize T2D, designed to evaluate Revita in multiple concurrent clinical studies across a range of patient populations from prediabetes to T2D patients on long-acting insulin. In addition, we are developing Rejuva, a novel pancreatic gene therapy platform, to enable long-term remission of T2D by potentially restoring insulin production in patients with advanced disease. We believe our product candidates, if approved, have the potential to revolutionize the treatment of T2D, align the interest of key stakeholders in the disease, and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

T2D is a disorder of rising blood glucose that is caused by a multitude of factors, which lead to two parallel, progressive disease processes within the body: insulin resistance and insulin insufficiency. Insulin resistance is the body's inability to respond appropriately to an insulin signal to remove glucose from the bloodstream, whereas insulin insufficiency is the gradual failure of the pancreas to produce sufficient insulin to meet the body's needs. Guidelines today focus on managing the blood glucose symptoms of T2D, often measured by blood concentrations of glycosylated hemoglobin, or HbA1c, rather than attempting to correct the underlying pathology in the body causing insulin resistance and insulin insufficiency. We believe the current symptom-driven approach to T2D management is misdirected and unreasonable. It asks patients for dietary and lifestyle changes in the face of an altered physiologic set-point in the body, rigorous and lifelong patient adherence and persistence to medicines, and unquestioning willingness to accede to increasingly complex therapies. This burdensome approach to care is often unmanageable and may leave many patients at risk, potentially resulting in chronic elevations in blood glucose that increase the likelihood of microvascular and macrovascular complications of T2D, and even death. There are no therapies that are approved today in T2D that offer disease modification, which we define as ongoing and durable preservation of pancreatic insulin production capacity even after therapy is discontinued.

We believe that recent advances in our understanding of the dysfunction of key metabolic organs now enable the development of new disease-modifying approaches aimed at reversing T2D. Our founders first identified an organ-level pathology of a segment of the intestine, called the duodenum, that may become

dysfunctional by the direct impact of modern diets high in fats and sugars. We believe these diets lead to structural and functional pathology of the duodenal mucosa, alter the neurohormonal signal from the gut to the brain and rest of the body, and shift the body's metabolic set-point toward obesity and insulin resistance. Interventions that reduce duodenal nutrient sensing and signaling by a variety of means, such as gastric bypass surgery, have been shown to improve insulin resistance and insufficiency, resulting in lowered HbA1c and reduced risk of developing T2D. Together, we believe these observations help position gut dysfunction as a target for therapy at the apex of the metabolic disease cascade within the body, potentially enabling protection from insulin resistance, obesity and beta cell dysfunction in T2D.

Our Solution: Revita

Revita is designed to target the organ-level root cause of T2D in the duodenum with an endoscopic procedure. We believe Revita's unique features have the potential to provide a significantly differentiated and compelling solution to the large unmet need in T2D. If successful, we believe Revita could fundamentally disrupt the chronic care model for patients with or at risk for T2D, and could offer the following potential benefits:

- ***Real World Outcomes.*** Revita does not rely on perfect patient adherence or persistence to chronic therapy for its anticipated clinical effects because it is a procedural therapy, unlike diet and lifestyle interventions or pharmacologic management.

- ***Broad Implementation.*** Revita leverages familiar skillsets of advanced endoscopists, can potentially be easily incorporated into endoscopist workflow, fits into most endoscopy suites, typically requires less than five cases for the endoscopist to acquire proficiency, and is designed to be an outpatient procedure that can be performed by a trained therapeutic endoscopist in less than an hour. In addition, in our clinical studies to date, over 95% of endoscopic procedures have successfully ablated the target treatment area.

- ***Patient Friendly.*** Revita is designed to offer a straightforward, outpatient, endoscopic procedural experience for patients, requiring less than a half-day visit, with the goal of allowing patients to typically return to their normal daily lives and work the next day.

- ***Significant Health Savings.*** Revita, in combination with at least one ongoing oral antidiabetic agent, or OAD, and lifestyle counseling, has been observed to have a statistically significant mean HbA1c reduction of 1.0% (n=27) and a statistically significant mean fasting plasma glucose reduction of 32 mg/dL (n=28) at 24 months in a long-term follow-up study of the per-protocol, or PP, population in our Revita-1 feasibility study. In addition, Revita, in combination with a glucagon-like peptide-1 receptor agonist and lifestyle counseling, has been observed to help eliminate the need for insulin in eight of 15 patients (statistically significant as compared to baseline) at 18 months in a long-term follow-up study of the PP population in our INSPIRE pilot study. Based on these observations, we believe Revita may help enhance disease control and thereby reduce pharmacological expenditure and improve health outcomes for patients and health systems.

- ***Disease Modification.*** Revita is designed to target and reduce the neurohormonal signal leading to insulin resistance, the underlying metabolic defect of T2D and other metabolic diseases.

- ***Tolerability.*** In clinical studies to date, Revita has been observed to be generally well tolerated, with most patients resuming normal daily activities one day after the procedure and none requiring prescription pain medications. We believe our proprietary SureLift technology enables isolation of the mucosa from deeper tissue structures, sparing pain fibers in the muscle and reducing risk of injury.

- ***Mechanism, Durability, Repeatability.*** Revita is designed to improve metabolic health, blood glucose levels, and weight in patients with inadequately controlled T2D. Based on a long-term follow-up study of the PP population in our Revita-1 study, we observed that Revita, in combination with at least one ongoing OAD and lifestyle counseling, had a statistically significant HbA1c reduction of 1.0% (n=27) and a statistically significant raw change in weight of -3.1 kg (n=25) in patients at 24 months. In addition, we believe our SureLift technology has the potential to enable repeat Revita procedures over time. After the commercial launch of Revita, if approved, we may conduct a post-approval study, or PAS, to evaluate the safety and effectiveness of potential repeat procedures, should they be necessary.

- ***Modular System.*** The Revita console is designed to support the duodenal mucosal resurfacing, or DMR, procedure and can also potentially be used to support our Rejuva gene therapy platform, which is designed to provide precise local delivery of gene therapy to the pancreas, in a single endoscopic procedure performed in a single setting.

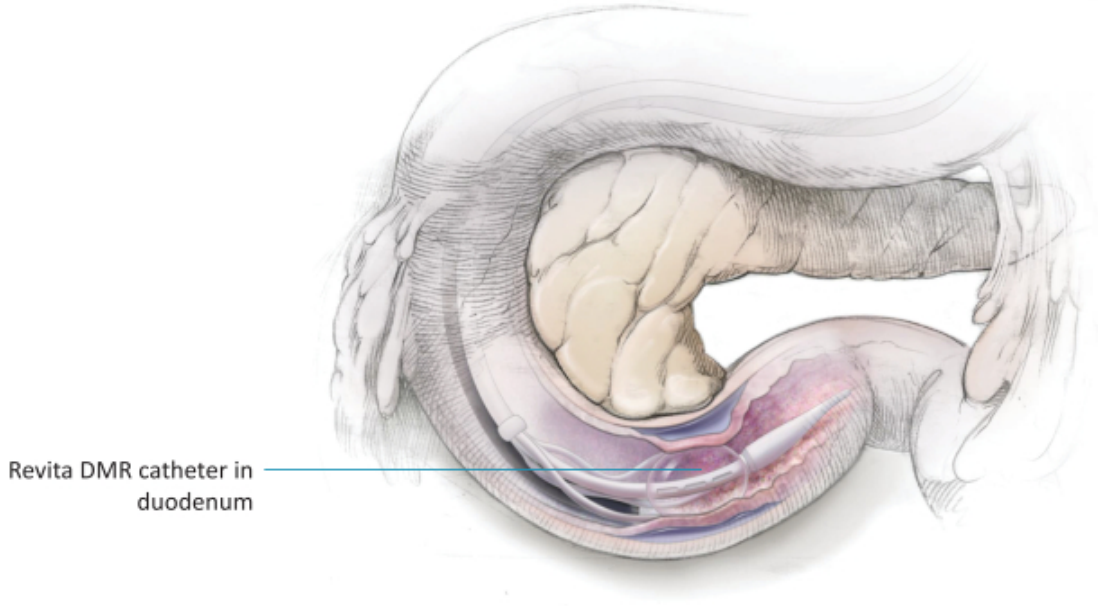
In March 2021, we initiated Revitalize-1, a pivotal clinical study of Revita in patients with inadequately controlled T2D despite being on metformin, up to two additional antidiabetic agents, or ADAs, and long-acting insulin, and expect topline data in 2024. If successful, we intend to submit a Premarketing Approval application, or PMA, to the U.S. Food and Drug Administration, or the FDA, for Revita to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin. We have received Investigational Device Exemption, or IDE, approval from the FDA to initiate Revitalize-2, a pivotal study in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy and plan to initiate this study in the second half of 2022. In addition, we plan to initiate Revitalize-3, a proof-of-concept pilot study in patients with a high risk of prediabetes, in 2022.

The image below depicts a prototype rendering of the modular Revita console with the current touchscreen user interface. The catheter and graphical user interface are currently being used in our Revitalize-1 clinical study but the Revita console hardware below is not. We plan to seek approval from the FDA of a supplemental premarket approval application, or PMA, for this console design modification.

Modular Revita Console Powered by an Intuitive Touchscreen User Interface

Revita utilizes a proprietary endoscopic catheter-based approach with control hardware and software with a two-step procedure of (1) thermal isolation of the duodenal mucosa, and then (2) hydrothermal energy delivery to ablate the mucosal surface. The objective of therapy is to disrupt the dysfunctional duodenal neurohormonal signal and allow the rapid regeneration of a new mucosa. To date, Revita has been evaluated in approximately 300 patients across multiple clinical studies and we have observed over 500 patient-years of exposure data across these clinical studies in T2D. The image below illustrates the Revita DMR catheter performing SureLift on the duodenal mucosa.

Revita DMR Catheter



We obtained a Conformitè Europëenne, or CE, mark for Revita in Europe in 2016 for the improvement of glycemic control in patients with inadequately controlled T2D despite oral and/or injectable glucose lowering medications and/or long-acting insulin, although we do not currently market Revita in any territory. In 2022, the Institute for the Hospital Renumeration System (Germany) granted Revita Status 1 designation under its new examination and treatment methods, or NUB, funding process whereby hospitals that submitted a NUB application are now entitled to negotiate reimbursement for the use of Revita in clinical studies and/or real-world evidence generation in a commercial setting. In the United States, we obtained a Breakthrough Device designation from the FDA for Revita in 2021 to perform hydrothermal ablation of the duodenal mucosa, or the Revita DMR Procedure, to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin. Breakthrough Device designation provides certain benefits to device developers, including more interactive and timely communications with FDA staff, use of post-market data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design, and prioritized review of premarket submissions but does not alter or confer any advantage in the regulatory review or approval standard for medical devices. We are currently enrolling patients for the Revitalize-1 pivotal study in the United States and the EU, and plan to initiate the Revitalize-2 pivotal study in the second half of 2022. In 2022, we also intend to submit an IDE to the FDA or comparable documents to other regulatory authorities for the Revitalize-3 pilot study. If we are successful in developing Revita for certain indications in T2D and prediabetes, we believe Revita could also

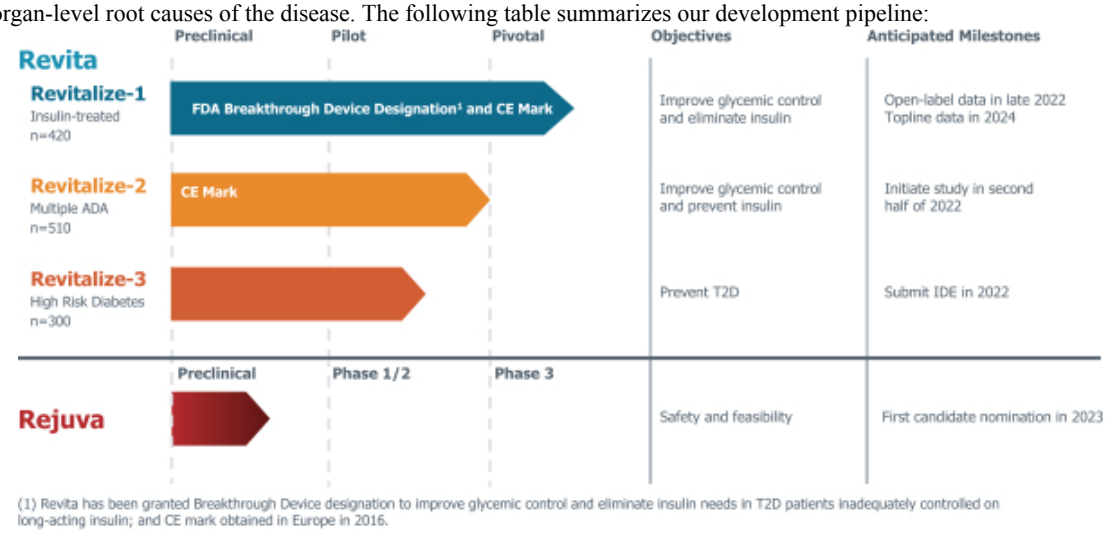
have the potential to be developed for expanded indications for use in a broader population of patients in other serious diseases, including cardiovascular disease, or CVD, polycystic ovary syndrome and nonalcoholic fatty liver disease, among others.

Our Solution: Rejuva

Our novel Rejuva gene therapy platform is designed to restore insulin production capacity in the pancreas via endoscopic, locally delivered adeno-associated virus, or AAV, mediated gene therapy of key metabolic hormones necessary for proper insulin production in the beta cells of the pancreas. Our first gene therapy candidate in the Rejuva program will utilize glucagon-like peptide-1, or GLP-1, receptor analogues. We believe that augmenting GLP-1 receptor activation in the pancreas may lead to reductions in blood glucose through a mechanism distinct from that of the DMR procedure and as an adjunct to Revita. We plan to develop this platform initially for the treatment of advanced, insulin-treated T2D. In a proof-of-concept preclinical study in a diabetic mouse model, we observed a statistically significant average reduction of fasting blood glucose levels of 54% ($p < 0.0001$) and a statistically significant increase in insulin production of 38% ($p < 0.01$) during a glucose tolerance test at a 5-week time point after a single administration of a certain Rejuva platform gene therapy candidate compared to the control vector. No evidence of safety signals to the pancreas or liver were observed in the study. We anticipate nominating our first gene therapy candidate for our Rejuva program and initiating IND-enabling studies in 2023.

Our Development Pipeline

Our development pipeline aims to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. The following table summarizes our development pipeline:



(1) Revita has been granted Breakthrough Device designation to improve glycemic control and eliminate insulin needs in T2D patients inadequately controlled on long-acting insulin; and CE mark obtained in Europe in 2016.

Our Team

We were founded by our Chief Executive Officer, Harith Rajagopalan, M.D., Ph.D., and our Chief Product Officer, Jay D. Caplan, with the goal of developing innovative procedures and novel therapeutics to improve the lives of patients with metabolic diseases, initially targeting T2D. Before starting Fractyl Health,

Dr. Rajagopalan was a physician scientist and cardiovascular fellow at Brigham and Women's Hospital. During his M.D./Ph.D. training at Johns Hopkins, Dr. Rajagopalan did award winning research on mechanisms of colorectal cancer formation with significant implications on cancer metabolism and published in leading scientific journals, including *Nature* and *Science*. Dr. Rajagopalan's background in cancer metabolism, cardiovascular medicine and stem cell biology research has contributed to the founding scientific insight behind Fractyl Health: intestinal stem cell biology fundamentally helps to explain one of the root causes of obesity and metabolic disease in humans, along with the attendant health consequences, including T2D, CVD and colorectal cancer. Jay Caplan is an electrical engineer by training and an experienced life sciences executive with an extensive track record of developing transformational medical products, including at ThermoCardio with the development of the HeartMate 2 Left Ventricular Assist Device. Our multi-disciplinary team consists of both seasoned biopharmaceutical and medical device professionals with deep industry experience. Our team brings together experts across multiple areas, including endocrinology (particularly in metabolic diseases), gastroenterology, endoscopy, engineering and medical device development. Members of our team have worked with well-regarded biopharmaceutical and medical technology companies, such as Pfizer, AbbVie and Abbott, and we are supported by a leading group of life sciences investors.

What Sets Us Apart

Our vision is to transform the care of chronic metabolic diseases from the current practice of daily blood glucose management to the treatment of the root causes of T2D and related diseases. Our culture of scientific rigor and innovation is entrenched in all aspects of our organization and informs our goal of disrupting the current inadequate standard of care. While no products that target the gut or the pancreas have been approved, we are focused on developing disease-modifying therapies to treat metabolic diseases by targeting these organs, driving widespread adoption of our novel approach, delivering on the promise of improved experience for patients and health systems, and also potentially reducing costs for the healthcare system. We believe our vision is supported by the following strengths:

- ***Pioneering a New Approach Based on Deep Understanding of Metabolic Diseases.*** Our mission is to pioneer the investigation and understanding of the gut as a root cause of metabolic disease. Our approach builds on over a decade of our research and the accumulation of independently published, supportive clinical evidence from gastric bypass surgeries, all implicating the gut as a validated, untapped target in metabolic disease. We focus our product innovation on targeting the gut and other key organs implicated in the pathogenesis of T2D and related metabolic diseases, with the aim of restoring and preserving the health of the key organs required for metabolic fitness and reducing the burden of metabolic disease for patients and society.

- ***Developing a Disease-Modifying Procedural Therapy for T2D.*** Our lead product candidate, Revita, is designed to disrupt nutrient absorption and address the abnormal neurohormonal signals in the duodenum by targeting and ablating the diseased mucosa in patients with T2D, which has not been attempted previously. In 2021, the FDA granted Revita Breakthrough Device designation to improve glycemic control and eliminate insulin in T2D patients inadequately controlled on long-acting insulin, which could potentially expedite the development and lead to prioritized FDA review of Revita. Assuming regulatory approval and adoption by key stakeholders, we believe Revita has the potential to address the core weaknesses in the current T2D treatment paradigm and provide long-term clinical benefits to T2D patients by potentially improving overall glycemic control and quality of life while reducing the burden of chronic disease management.

- ***Rigorous Approach to Evaluating Revita.*** Our broad clinical program, Revitalize T2D, is designed to advance the development of Revita to potentially become a backbone procedural therapy across the spectrum of T2D. To date, we have evaluated Revita in approximately 300 patients across multiple clinical studies and we have observed over 500 patient-years of exposure data, favorable

tolerability data, as well as favorable glycemic control data. The Revitalize T2D program is designed to evaluate our lead product candidate in multiple concurrent clinical studies across a range of T2D patient populations.

- ***Aligning Interests of Key Stakeholders: Patients, Referring Physicians, Providers and Payors.*** We believe Revita, if approved, has the potential to offer clinical and societal benefits while reducing the burden of disease management compared to the current standard of care in T2D. We believe that the successful completion of our clinical studies of Revita, publication of scientific and medical results in peer-reviewed journals, and presentation of data at leading conferences are critical to the clinical and commercial adoption of Revita, if approved. We believe Revita has the potential to broadly align interests across key stakeholders involved in the treatment of T2D, and may have the following benefits to these groups:

  - *Patients.* Improving glycemic control while reducing the number and burden of therapies required to adequately control T2D.

  - *Referring Physicians.* Lowering HbA1c for specific patient populations with a procedural therapy, without the escalating need to rely on rigorous patient medication or diet adherence and persistence to medicines, or willingness to accede to increasingly complex and burdensome therapies.

  - *Providers.* Straightforward, easy to train outpatient procedure, which we believe could be safely deployed at scale across a large patient population. Intended to seamlessly integrate into existing endoscopist workflows and provide a new, profitable service line for hospitals with a patient-friendly therapeutic option for a significant fraction of their patients.

  - *Payors.* Significant health economic benefits for payors who are currently struggling with the increasing expenses of T2D, driven primarily by unchecked disease progression and the lack of disease-modifying therapies.

- ***Purpose-Built Leadership Team with Shared Mission to Address Root Cause of Metabolic Diseases.*** We are mission-driven to develop novel disease-modifying procedural therapies that can potentially reverse metabolic diseases for patients and for health systems. Our team aims to continuously advance and expand upon our body of knowledge in order to establish and maintain a scientific leadership position in our therapeutic areas of focus. We do so by collaborating with expert advisors who are leaders in metabolic disease, endocrine signaling and endoscopy. As part of these ongoing efforts, we have also convened the Erase T2D Task Force, a group of academic and scientific experts in the metabolic disease space, to serve as key advisors as we develop our understanding of the role of the gut in T2D. The Erase T2D Task Force is co-chaired by our CEO, Harith Rajagopalan, M.D., Ph.D., and Alan Cherrington, Ph.D., the former President of the American Diabetes Association and the winner of its Banting Medal for Scientific Achievement.

Growth Strategies

We intend to build a high growth business that is sustainable, predictable and profitable over time. In order to achieve this goal, we plan to employ the following strategies:

- ***Establish Practice-Changing Levels of Evidence Across the Spectrum of T2D***.

- ***Execute Targeted and Efficient Go-to-Market Strategy***.

- ***Expand the Indication and Use of Revita***.

- ***Develop Rejuva Gene Therapy Platform to Enable Long-Term Remission of T2D by Restoring Insulin Production in Patients with Advanced Disease***.

- ***Broaden Geographic Footprint for Revita***.

Summary Risk Factors

Investing in our common stock involves substantial risk. Our ability to execute our strategy is also subject to certain risks. The risks described under the heading "Risk Factors" included elsewhere in this prospectus may cause us not to realize the full benefits of our strengths or may cause us to be unable to successfully execute all or part of our strategy. Some of the most significant challenges and risks include the following:

- We have a limited operating history in developing medical devices and biopharmaceutical products, have not completed any pivotal clinical studies and have no products approved for commercial sale in the United States, which may make it difficult for you to evaluate our current business and predict our future success and viability.

- We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future and may never achieve or sustain profitability.

- Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

- The regulatory approval process of the FDA, comparable foreign regulatory authorities and notified bodies, are lengthy, time-consuming and inherently unpredictable, and even if we complete the necessary clinical studies, we cannot predict when, or if, we will obtain regulatory approval or certification for any of our product candidates, and any such regulatory approval or certification may be for a more narrow indication than we seek.

- We may not be able to file IDEs or IDE supplements or comparable documents in foreign jurisdictions to commence additional clinical studies on the timelines we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed.

- Our product candidates may cause serious adverse events or undesirable side effects or have other properties which may cause us to suspend or discontinue clinical studies, delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

- We are substantially dependent on the success of our lead product candidate, Revita. If we are unable to obtain marketing approval or certification for and commercialize any of our current or future product candidates in a timely manner, our business will be harmed.

- We may not be able to gain the support of leading hospitals and key thought leaders, or to publish the results of our clinical studies in peer-reviewed journals, which may make it difficult to establish the Revita DMR Procedure and/or our Rejuva gene therapy candidate as a standard of care, if approved, and may limit our revenue growth and ability to achieve profitability.

- We have not yet studied the ability of Revita to be used in repeated procedures and we are uncertain as to whether patients will need additional procedures in the future. If we are unable to demonstrate the safety and improved glycemic effects of Revita for repeat use, it could have a material adverse effect on the on the clinical utility and commercial adoption of the device.

- We have never obtained marketing approval for a product candidate in the United States or abroad and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any product candidate in the United States.

- Although Revita has received Breakthrough Device designation, there can be no guarantee that the designation will benefit the development and regulatory approval process.

- If we are unable to obtain a billing code from the U.S. Department of Health and Human Services so that procedures using Revita, if approved, are covered under Medicare and Medicaid, this could have a negative impact on our intended sales and would have a material adverse effect on our business, financial condition and operating results.

- The training required for endoscopists to use Revita could reduce the market acceptance of our products, when and if approved.

- The COVID-19 pandemic and potential future pandemics could continue to adversely impact our business, including our anticipated clinical studies, supply chain and business development activities.

- We substantially rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct certain aspects of our preclinical studies, and clinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain marketing authorization of or commercialize our product candidates and our business could be substantially harmed.

- We contract with third parties for the manufacture of sub-assembly components for Revita and for the materials for our Rejuva gene therapy platform for preclinical studies and our ongoing clinical studies, and expect to continue to do so for additional clinical studies and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- We rely on a variety of intellectual property rights, and if we are unable to obtain, maintain or protect our intellectual property, our business, financial situation, results of operations, and prospects will be harmed. If we are unable to obtain and maintain patent protection for our current product candidate, any future product candidates we may develop and our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our current product candidate, any future product candidates we may develop and our technology may be adversely affected.

Corporate History and Information

We were incorporated under the laws of the state of Delaware on August 30, 2010 under the name MedCatalyst, Inc. On January 12, 2012, we changed our name to Fractyl Laboratories Inc. On June 9, 2021, we

changed our name to Fractyl Health, Inc. Our principal executive offices are located at 17 Hartwell Avenue, Lexington, Massachusetts 02421 and our telephone number is (781) 902-8800. Our principal website address is *www.fractyl.com*. The information on or accessed through our website is not incorporated in this prospectus or the registration statement of which this prospectus forms a part.

Recent Developments

In January 2022, we sold and issued approximately $20.1 million aggregate principal amount of convertible promissory notes, or the 2022 Notes, in a private placement transaction. The 2022 Notes accrue interest at a rate of 3.0% per annum and will automatically settle into shares of our common stock in connection with the closing of this offering at a price equal to the lesser of (i) 80% of the initial public offering price per share set forth on the cover page of this prospectus or (ii) a price per share equal to $1.1 billion divided by our fully diluted capitalization as of immediately prior to the closing of this offering.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. As an "emerging growth company" we may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- the option to present only two years of audited financial statements and only two years of related "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act;
- not being required to comply with any requirements that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (i.e., an auditor discussion and analysis);
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until the last day of our fiscal year following the fifth anniversary of the completion of this offering. However, if any of the following events occur prior to the end of such five-year period, (i) our annual gross revenue exceeds $1.07 billion, (ii) we issue more than $1.0 billion of non-convertible debt in any three-year period, or (iii) we become a "large accelerated filer," (as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act), we will cease to be an emerging growth company prior to the end of such five-year period. We will be deemed to be a "large accelerated filer" at such time that we (a) have an aggregate worldwide market value of common equity securities held by non-affiliates of $700.0 million or more as of the last business day of our most recently completed second fiscal quarter, (b) have been required to file annual and quarterly reports under the Exchange Act, for a period of at least 12 months, and (c) have filed at least one annual report pursuant to the Exchange Act. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting

company," which would allow us to take advantage of many of the same exemptions from disclosure requirements including reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests. In particular, we have elected to use the extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company, or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates. If we were to subsequently elect instead to comply with these public company effective dates, such election would be irrevocable pursuant to the JOBS Act.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

THE OFFERING

Common stock offered by us	shares
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase up to additional shares of common stock.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full)
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million (or approximately $ million if the underwriters exercise their option to purchase additional shares in full), based on an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds of this offering to fund the ongoing Revitalize-1 pivotal clinical study of Revita, the Revitalize-2 pivotal study, and the Revitalize-3 pilot study; the continued preclinical development of our Rejuva gene therapy platform; for medical education and market development, and other commercial readiness activities; and for working capital and other general corporate purposes. For a more complete description of our intended use of the proceeds from this offering, see "Use of Proceeds."
Risk factors	You should read the section titled "Risk Factors" beginning on page 16 and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Proposed Nasdaq Global Market symbol	"GUTS."

The number of shares of our common stock to be outstanding after this offering is based on shares of our common stock outstanding as of December 31, 2021, after giving effect to (i) the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock immediately prior to the closing of this offering and (ii) the issuance of shares of common stock upon the automatic settlement of the 2022 Notes, including accrued interest, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, in connection with the closing of this offering, and excludes:

- 17,738,374 shares of our common stock issuable upon exercise of outstanding stock options granted under the Fractyl Health, Inc. Amended and Restated 2011 Incentive Stock Plan, or the 2011 Plan, as of December 31, 2021, at a weighted average exercise price of $1.51 per share;
- 4,131,844 shares of our common stock available for future issuance under the 2011 Plan as of December 31, 2021, which such shares will cease to be available for issuance at the time our 2022 Plan (as defined below) becomes effective;

- shares of common stock that will become available for future issuance under the 2022 Incentive Award Plan, or the 2022 Plan, which will become effective in connection with the completion of this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2022 Plan;

- shares of common stock that will become available for future issuance under the 2022 employee stock purchase plan, or the ESPP, which will become effective in connection with the completion of this offering, and shares of our common stock that become available pursuant to provisions in the ESPP that automatically increase the share reserve under the ESPP; and

- 465,315 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2021, at a weighted average exercise price of $1.53 per share.

Unless we indicate otherwise or the context otherwise requires, all information in this prospectus assumes or gives effect to:

- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, each of which will occur immediately prior to the closing of this offering;

- the conversion of all outstanding shares of our convertible preferred stock into 77,994,156 shares of our common stock immediately prior to the closing of this offering;

- the conversion of 118,483 outstanding warrants to purchase shares of Series B Preferred Stock into 118,483 warrants to purchase shares of common stock immediately prior to the closing of this offering;

- the issuance of shares of common stock upon the automatic settlement of the 2022 Notes, including accrued interest, assuming an initial public offering price of $, which is the midpoint of the price range set forth on the cover page of this prospectus, in connection with the closing of this offering;

- a for stock split of our common stock, effected on , 2022;

- no exercise of the outstanding stock options or warrants described above after December 31, 2021; and

- no exercise by the underwriters of their option to purchase additional shares of our common stock.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables set forth our summary consolidated financial data for the periods indicated. We have derived the consolidated statements of operations data for the years ended December 31, 2021 and 2020 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected for any future period. You should read the following summary consolidated financial data together with the more detailed information contained in "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus.

(in thousands, except for share and per share information)	Year Ended December 31, 2021	2020
Consolidated Statements of Operations Data:		
Operating expenses:		
Research and development	$ 26,435	$ 22,433
General and administrative	10,493	6,528
Total operating expenses	36,928	28,961
Loss from operations	(36,928)	(28,961)
Other expenses, net		
Interest expense, net	(1,442)	(1,503)
Change in fair value of convertible preferred stock warrant liability	(356)	(15)
Other expenses, net	(9)	(1)
Total other expenses, net	(1,807)	(1,519)
Net loss and comprehensive loss	$ (38,735)	$ (30,480)
Accretion of dividends on convertible preferred stock	(14,486)	(10,422)
Net loss attributable to common stockholders	(53,221)	(40,902)
Net loss per share attributable to common stockholders, basic and diluted	$ (13.34)	$ (10.34)
Weighted average number of common shares outstanding, basic and diluted	3,990,680	3,955,147
Pro Forma net loss per share, basic and diluted (unaudited)(1)	$ (0.51)	$ (0.45)
Pro Forma weighted average shares of common stock outstanding, basic and diluted (unaudited)	76,662,137	67,112,431

(1) The unaudited pro forma net loss per share for the years ended December 31, 2021 and 2020 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of our convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates, if later.

(in thousands)	As of December 31, 2021 Actual	Pro Forma(1) (unaudited)	Pro Forma As Adjusted(2) (3) (unaudited)
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 95,473	$	$
Working capital(4)	72,734		
Total assets	102,548		
Total liabilities	24,543		
Accumulated deficit	(223,072)		
Convertible preferred stock	287,330		
Total stockholders' equity (deficit)	(209,325)		

(1) Gives effect to (i) the repayment in full of all outstanding borrowings under our Loan and Security Agreement in January 2022 for a total amount of $16.1 million, (ii) the receipt of approximately $20.1 million in cash proceeds from the sale of the 2022 Notes in January 2022, (iii) the automatic settlement of the 2022 Notes, including accrued interest, into shares of our common stock in

connection with the closing of this offering, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus, (iv) an aggregate charge to accumulated deficit of $ relating to the loss resulting from the settlement of the 2022 Notes, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus, and (v) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 77,994,156 shares of common stock immediately prior to the closing of this offering, as if such conversion had occurred on December 31, 2021.

(2) Gives further effect to the sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity (deficit) by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A 1.0 million share increase (decrease) in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity (deficit) by $ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. This information is illustrative only and will depend on the actual initial public offering price and other terms of this offering determined at pricing.

(4) We define working capital as current assets less current liabilities. See our financial statements and the related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

RISK FACTORS

You should carefully consider the risks and uncertainties described below and the other information in this prospectus, including our consolidated financial statements and related notes appearing elsewhere in this prospectus and in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. This prospectus also contains forward-looking statements that involve risks and uncertainties. See "Cautionary Note Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.

Risks Related to Our Financial Condition and Capital Requirements

We have a limited operating history in developing medical devices and biopharmaceutical products, have not completed any pivotal clinical studies and have no products approved for commercial sale in the United States, which may make it difficult for you to evaluate our current business and predict our future success and viability.

Medical device and biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are an organ-editing metabolic therapeutics company with a limited operating history in developing medical devices and biopharmaceutical products, which makes it difficult to evaluate our business and prospects in future product development. We have no products approved for commercial sale in the United States and have not generated any revenue from product sales. We obtained a CE mark for Revita in Europe in 2016. However, we do not currently market this product in any territory. To date, we have devoted substantially all of our resources and efforts to increasing our manufacturing capacity, raising capital, discovering, identifying and developing potential product candidates, securing related intellectual property rights and undertaking preclinical and clinical studies of our product candidates, including the ongoing Revitalize-1 pivotal clinical study of Revita for T2D patients that are inadequately controlled on metformin, up to two additional ADAs, and long-acting insulin. We have not yet demonstrated our ability to successfully complete any pivotal clinical studies, submit a Premarket Approval application, or PMA, a new drug application, or NDA, or biologic license application, or BLA, or similar marketing authorization application, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for you to accurately predict our future success or viability to develop new medical devices and biopharmaceutical products than it could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by medical device and biopharmaceutical companies developing products in rapidly evolving fields. We also may need to transition from a company with a research focus to a company capable of supporting commercial activities. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future and may never achieve or sustain profitability.

We have incurred net losses since inception, have not generated any revenue from product sales to date and have financed our operations primarily through the sale of our convertible preferred stock and debt financing. We have incurred a net loss of approximately $38.7 million and $30.5 million for the years ended December 31, 2021 and December 31, 2020, respectively. As of December 31, 2021, we had an accumulated deficit of approximately $223.1 million. Our losses have resulted principally from expenses incurred in research and development of our product candidates, from management and administrative costs and other expenses that

we have incurred while building our business infrastructure. Our lead product candidate, Revita, is currently undergoing a pivotal clinical study for T2D patients that are inadequately controlled on metformin, up to two additional ADAs, and long-acting insulin, and we expect to initiate a pivotal clinical study of Revita in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy in the second half of 2022. We expect that it will be several years, if ever, before we have a commercialized product and generate revenue from product sales. Even if we succeed in receiving marketing approval or certification for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses as we discover, develop and market additional potential product candidates.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- advance the development of our lead product candidate, Revita, and our Rejuva gene therapy candidate through preclinical and clinical development, and, if approved or certified by the FDA, other comparable foreign regulatory authorities or notified bodies, commercialization;
- incur manufacturing costs for our product candidates;
- increase our manufacturing capacity;
- seek regulatory approvals or certifications for any of our product candidates that successfully complete clinical studies;
- increase our research and development activities to identify and develop new product candidates;
- hire additional personnel;
- expand our operational, financial and management systems;
- invest in measures to protect and expand our intellectual property;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval and intend to commercialize;
- expand our manufacturing and develop our commercialization efforts; and
- operate as a public company.

To date, we have not generated any revenue. To become and remain profitable, we must succeed in developing and eventually commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical and clinical studies of our product candidates, obtaining regulatory approval, and manufacturing, marketing and selling any product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We may never succeed in these activities and, even if we do, may never generate any revenue or revenue that is significant enough to achieve profitability.

The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital and our ability to achieve and maintain profitability.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

Developing medical devices or biopharmaceutical products, including conducting preclinical and clinical studies, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we initiate and conduct clinical studies of, and seek marketing approval or certification for our current and any future product candidates. Even if one or more of the product candidates that we develop is approved or certified for commercial sale, we anticipate incurring significant costs associated with commercializing any approved or certified product candidate. Our expenses could increase beyond expectations if we are required by the FDA or other comparable foreign regulatory authorities or notified bodies to perform clinical studies or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. In addition, if we obtain marketing approval or certification for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Because the design and outcome of our anticipated clinical studies are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate we develop. Following this offering, we also expect to incur additional costs associated with operating as a public company. Accordingly, it is likely that we will need to obtain substantial additional funding in order to maintain our continuing operations in the future.

As of December 31, 2021, we had approximately $95.5 million in cash and cash equivalents. Based on our current business plans, we believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operating expenses and capital expenditures requirements through . Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash and cash equivalents, to be able to continue to fund our operating expenses and capital expenditures requirements is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

Our future funding requirements will depend on many factors, including, but not limited to:

- the initiation, progress, timeline, cost and results of our clinical studies for our product candidates;
- the initiation, progress, timeline, cost and results of additional research and preclinical studies related to pipeline development and other research programs we initiate in the future;
- the cost and timing of manufacturing activities as we advance our product candidates through clinical development and commercialization;
- the potential expansion of our current development programs to seek new indications;

- the continued negative impact of the COVID-19 pandemic or future health crises, including epidemics and pandemics, on our business;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities or notified bodies;
- the ability of healthcare providers to obtain coverage and adequate reimbursement by third-party payors for procedures using our products, if approved, and any additional products we commercialize, as well as any future changes to coverage or reimbursement policies that may increase our competition or reduce reimbursement for procedures using our products, if approved;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights, in-licensed or otherwise;
- the effect of competing technological and market developments;
- the payment of licensing fees, potential royalty payments and potential milestone payments;
- the cost of general operating expenses;
- the cost and timing of completion of commercial-scale manufacturing and product development activities;
- market acceptance of our product candidates, if cleared, approved or certified;
- the cost of establishing sales, marketing, and distribution capabilities for any product candidates for which we may receive regulatory approval or certification in regions where we choose to commercialize our products, if approved, on our own; and
- the cost of operating as a public company.

We plan to use the net proceeds from this offering to fund the ongoing Revitalize-1 pivotal clinical study of Revita, the Revitalize-2 pivotal study, and the Revitalize-3 pilot study; the continued preclinical development of our Rejuva gene therapy platform; for medical education and market development, and other commercial readiness activities; and for working capital and other general corporate purposes. Advancing the development of our product candidates will require a significant amount of capital. The net proceeds from this offering and our existing cash and cash equivalents will not be sufficient to fund all of the activities that are necessary to complete the development and commercialize our product candidates, if approved.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. Other than our Loan Agreement, we do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Additionally, the impact of the COVID-19 pandemic on the capital markets may affect the availability, amount and type of financing available to us in the future. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical studies or future commercialization efforts.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates on unfavorable terms to us.

We may seek additional capital through a variety of means, including through public or private equity offerings, debt financings or other sources, including up-front payments and milestone payments from strategic collaborations. To the extent that we raise additional capital through the sale of equity or convertible debt or equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Such financing may result in dilution to stockholders, imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through up-front payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our ability to utilize our net operating loss carryforwards, research and development tax credit carryforwards, and certain other tax attributes to offset taxable income or taxes may be limited.

As of December 31, 2021, we had U.S. federal and state net operating loss carryforwards of approximately $198.9 million and $194.6 million, respectively, which begin to expire at various dates beginning in 2030. Portions of these net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the legislation enacted in 2017, commonly referred to as the Tax Cuts and Jobs Act, or the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security, or the CARES Act, U.S. federal net operating losses incurred in taxable years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal net operating losses in taxable years beginning after December 31, 2020, is limited. It is uncertain how various states will respond to the Tax Act and the CARES Act.

In addition, as of December 31, 2021, we had U.S. federal and state research and development tax credit carryforwards of $6.5 million and $2.7 million, respectively. The federal research and development tax credit carryforwards will expire at various dates beginning in 2031. The state research and development tax credit carryforwards will expire at various dates beginning in 2027. We may not be able to utilize these credits for federal and state income tax purposes before they expire.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. The completion of this offering, together with other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382. To date, we have not completed an analysis under Section 382. We may experience ownership changes as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future results of operations by effectively increasing our future tax obligations.

Risks Related to Development, Regulatory Approval and Commercialization

The regulatory approval process of the FDA, comparable foreign regulatory authorities and notified bodies, are lengthy, time-consuming and inherently unpredictable, and even if we complete the necessary clinical studies, we cannot predict when, or if, we will obtain regulatory approval or certification for any of our product candidates, and any such regulatory approval or certification may be for a more narrow indication than we seek.

The research, testing, manufacturing, labeling, approval, certification, selling, import, export, marketing, and distribution of medical devices and biopharmaceutical products are subject to extensive regulation by the FDA and other regulatory authorities in and outside the United States. We are currently in clinical-stage development of Revita, which is an investigational medical device, and are conducting preclinical development of our Rejuva gene therapy candidate along with its device delivery system, which together with the gene therapy candidate, we anticipate will be regulated as a combination biologic-device.

In the United States, before we can market a new medical device, we must first receive either clearance under Section 510(k) of the Federal Food, Drug, and Cosmetic Act, or the FDCA, or approval of a PMA, from the FDA, unless an exemption applies. We expect Revita to be subject to the requirement for approval of a PMA. In the process of obtaining PMA approval, the FDA must determine that a proposed device is safe and effective for its intended use based, in part, on extensive data, including, but not limited to, technical, preclinical, clinical, manufacturing and labeling data. The PMA process is typically required for devices that are deemed to pose the greatest risk, such as life sustaining, life supporting or implantable devices. We plan to seek approval of a PMA from the FDA for the Revita DMR Procedure to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin.

Modifications to products that are approved through a PMA generally require FDA approval. Both the PMA approval and the 510(k) clearance process can be expensive, lengthy and uncertain. The process of obtaining a PMA is costly and uncertain and generally takes from one to three years, or even longer, from the time the application is submitted to the FDA. In addition, a PMA generally requires the performance of one or more clinical studies. Despite the time, effort and cost, a device may not be approved by the FDA. Any delay or failure to obtain necessary regulatory approvals could harm our business. Furthermore, even if we are granted regulatory approvals, they may include significant limitations on the indicated uses for the device, which may limit the market for the device.

Similarly, we are not permitted to market any biological product in the United States or in foreign jurisdictions until we receive approval of a biologics license application, or BLA, from the FDA or approval of similar foreign applications from comparable foreign authorities. We anticipate that our Rejuva gene therapy candidate will be regulated as a biological product or biological product-device combination product, requiring approval of a BLA or a similar approval from comparable foreign authorities, and as the case may be, certification from a notified body. We have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign authorities. A BLA and similar approval filings must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. The BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, including with respect to chain of identity and chain of custody of the product. Similar requirements may apply in foreign jurisdictions.

To the extent we intend to sell medical devices in member states of the European Union, or EU, our products must comply with the general safety and performance requirements of the Medical Devices Regulation, or MDR (Regulation (EU) No 2017/745). Compliance with these requirements is a prerequisite to be able to affix the European Conformity, or CE, mark to our products, without which they cannot be sold or marketed in the EU. See "Government Regulations—Regulation of Medical Devices in the European Union" for more information. To demonstrate compliance with the general safety and performance requirements, we must

undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. Except for low risk medical devices (Class I), where the manufacturer can self-assess the conformity of its products with the general safety and performance requirements (except for any parts which relate to sterility, metrology or reuse aspects), a conformity assessment procedure requires the intervention of a notified body. See "Government Regulations—Regulation of Medical Devices in the European Union" for more information.

In the EU, we must inform the notified body that carried out the conformity assessment of the medical devices that we market or sell in the EU, of any planned substantial changes to our quality system or substantial changes to our medical devices that could affect compliance with the general safety and performance requirements laid down in Annex I to the Medical Devices Regulation or cause a substantial change to the intended use for which the device has been CE marked. The notified body will then assess the planned changes and verify whether they affect the products' ongoing conformity with the Medical Devices Regulation. If the assessment is favorable, the notified body will issue a new certificate of conformity or an addendum to the existing certificate attesting compliance with the general safety and performance requirements and quality system requirements laid down in the Annexes to the Medical Devices Regulation.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA (which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland). Non-compliance with the above requirements would therefore also prevent us from selling our products, if approved, in Norway, Liechtenstein and Iceland .

The CE mark for Revita was issued under the Medical Devices Directive, or MDD, which has now been superseded by the MDR; however, there are transitional provisions which allow for devices which were authorized under the MDD to be placed on the market or put into service until May 26, 2025, provided that the requirements of the transitional provisions are fulfilled, or until their current certificate expires, if earlier. We have assessed our Quality Management System, or QMS, and technical file for compliance with the MDR, including device classification, reporting frequency and requirements and whether or not the current system complies with the general safety and performance requirements. In addition, the technical file was assessed for compliance by our Authorized Representative, Emergo. Lastly, QMS compliance to MDD and MDR is assessed by our notified body BSI. Throughout these assessments, there have been some QMS gaps, which were addressed with updated SOP's and by registering with EUDAMED and partnering with services in the EU for Authorized Representative (Emergo), Importer of Record (Medenvoy) and Data Protection Officer and legal representative (MWB). With respect to Revita, the essential requirements were updated to comply with the general safety and performance requirements and no gaps in the product were identified, with the exception of Unique Device Identification System, or UDI, compliance. UDI compliance for both the United States and internationally will be addressed in the first half of 2022. Based on the ongoing transition, work done to date, in conjunction with the ongoing and planned clinical program, we believe there is little risk that the product would not pass a conformity assessment. To that end, and in consideration with the certificate expiration date, we have developed a plan to address any identified gaps in the first half of 2022 and will file for a conformity assessment and re-certification in the second half of 2022, with an expected recertification in the first half of 2023, thus completing the transition a year prior certificate expiration, leaving plenty of time to address any identified non-conformance during the assessment and audit. In short, considering Revita is a Class IIb product, we believe the change to MDR has had little impact on how Revita is regulated throughout the EU and EEA. Nevertheless, we cannot be certain that the change to MDR will not have any material impact on the sale of Revita in the EU and, if we were considered noncompliant and unable to sell Revita in the EU, it could harm our business, operating results, prospects and financial condition.

As a result of the UK leaving the EU, since January 1, 2021, the regulatory framework and regimes for medical devices in the UK and EU have diverged. Northern Ireland has adopted a hybrid approach as a result of the divergence in accordance with the Northern Ireland Protocol. Great Britain's national legislation remains based on the MDD, however, until June 30, 2023, medical devices that have a CE mark can continue to be

marketed in Great Britain, provided that such devices are also registered with the Medicine and Healthcare products Regulatory Agency, or MHRA.

On January 1, 2021, the UK Conformity Assessed, or UKCA, mark was introduced for medical devices being placed on the Great Britain market. The UKCA mark is not recognized in the EU, EEA or Northern Ireland markets, so relevant products require a CE mark for sale in these markets.

Our product candidates could fail to receive regulatory approval or certification from the FDA, a comparable foreign regulatory authority or notified body for many reasons, including:

- disagreement with the design or conduct of our clinical studies;
- failure to demonstrate to the satisfaction of regulatory agencies or notified bodies that our product candidates are safe and effective, or have a positive benefit/risk profile for its proposed indication;
- serious and unexpected adverse device effects experienced by participants in our clinical studies;
- failure of clinical studies to meet the level of statistical significance required for approval or certification;
- disagreement with our interpretation of data from preclinical or clinical studies;
- the insufficiency of data collected from clinical studies of our product candidates to support the submission and filing of a IND, PMA or BLA or other submission or to obtain regulatory approval or certification;
- failure to obtain approval of our manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies or our own manufacturing facility; or
- changes in the approval or certification policies or regulations that render our preclinical and clinical data insufficient for approval or certification.

This lengthy approval process as well as the unpredictability of future clinical study results may result in our failing to obtain regulatory approval or certification to market our product candidates, which would significantly harm our business, results of operations and prospects. The FDA, a comparable foreign regulatory authority or notified body may require more information, including additional preclinical or clinical data to support approval or certification, which may delay or prevent approval or certification and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval or certification, regulatory authorities or notified bodies may approve or certify any of our product candidates for fewer or more limited indications than we request (including failing to approve or certify the most commercially promising indications), may grant approval contingent on the performance of costly post-marketing clinical studies, or may approve or certify a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Even if our product candidates meet their safety and efficacy endpoints in clinical studies, the regulatory authorities or notified bodies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval or certification.

We expect the novel nature of certain of our product candidates to create further challenges in obtaining regulatory approval or certification. The FDA may also require a panel of experts to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the panel, although not binding, may have a significant impact on our ability to obtain approval of the product candidates based on the completed clinical studies, as the FDA often adheres to the panel's recommendations. In addition, we may experience delays or

rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical studies and the review process. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

Clinical studies are expensive, time-consuming, difficult to design and implement, and have an uncertain outcome. Further, we may encounter substantial delays in our clinical studies.

Before obtaining regulatory approvals or certification for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical and clinical studies that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and takes many years to complete, and is subject to uncertainty. Our clinical studies may not be conducted as planned or completed on schedule, if at all. Failure can occur at any time during the clinical study process. Even if our clinical studies are completed as planned, their results may not support the safety and effectiveness of our product candidates for their targeted indications or support continued clinical development of such product candidates. Our future clinical study results may not be successful.

In addition, even if our planned studies are successfully completed, the FDA or foreign regulatory authorities or notified bodies may not interpret the results as we do, and more studies could be required before we submit our product candidates for approval or certification. To the extent that the results of the studies are not satisfactory to the FDA or foreign regulatory authorities or notified bodies for support of a marketing application or certification, we may be required to expend significant resources, which may not be available to us, to conduct additional studies in support of potential approval of our product candidates.

We may experience delays in conducting any clinical studies and we do not know whether our clinical studies will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient data to support the initiation of clinical studies;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical studies;
- delays in reaching agreement with the FDA or other regulatory authorities as to the design or implementation of our clinical studies;
- delays in or failure to obtain regulatory clearance to commence a clinical study;
- delays in or failure to reach an agreement on acceptable terms with clinical study sites or prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical study sites;
- delays in or failure to obtain IRB or ethics committee approval at each site;
- delays in or failure to recruit suitable patients to participate in a clinical study;
- delays in or failure to have patients complete a clinical study or return for post-treatment follow-up;
- clinical sites, CROs or other third parties deviating from study protocol or dropping out of a study;
- failure to perform in accordance with the FDA's good clinical practice, or GCP, requirements, or applicable regulatory guidelines in other countries;

- failure in addressing patient safety concerns that arise during the course of a study, including occurrence of adverse events associated with the product candidate;
- failure to add a sufficient number of clinical study sites; or
- failure to manufacture sufficient quantities of product candidates for use in clinical studies.

If we are required to conduct additional clinical studies or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical studies of our product candidates or other testing, if the results of these studies or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval or certification for our product candidates or not obtain marketing approval or certification at all;
- obtain marketing approval or certification in some countries and not in others;
- obtain marketing approval or certification for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval or certification with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval or certification.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned or ongoing clinical studies. We could encounter delays if a clinical study is suspended or terminated by us, by the IRBs of the institutions in which such studies are being conducted, by the Data Safety Monitoring Board, or DSMB, for such study or by the FDA or other regulatory authorities. These authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols, inspection of the clinical study operations or study site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical study. We may also seek feedback from the FDA or other regulatory authorities on our clinical development program, and the FDA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

We also cannot with any certainty whether or when we might complete a given clinical study. If we experience delays in the commencement or completion of our clinical studies, or if we terminate a clinical study prior to completion, the commercial prospects of our product candidates could be harmed, and our ability to generate revenues from our product candidates may be delayed. In addition, any delays in our clinical studies could increase our costs, slow down the development and approval or certification process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

We currently conduct and may in the future conduct clinical studies for our product candidates outside the United States, and the FDA or comparable foreign regulatory authorities may not accept data from such studies.

We are currently engaging in clinical studies that involve clinical sites in the United States and EU. We could also in the future plan to conduct one or more future clinical studies of our product candidates outside the United States, including in Europe. The acceptance of study data from clinical studies conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authorities may be subject to certain conditions or may not be accepted at all. In cases where data from clinical studies conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the studies were performed by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical study requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign studies would be subject to the applicable local laws of the foreign jurisdictions where the studies are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from studies conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable regulatory authority does not accept such data, it would result in the need for additional studies, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

We may not be able to file IDEs or IDE supplements or comparable documents in foreign jurisdictions to commence additional clinical studies on the timelines we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed.

In order to conduct a clinical investigation involving human subjects for the purpose of demonstrating the safety and effectiveness of a medical device, if necessary, for a PMA, 510(k) premarket notification or de novo classification request, a company must, among other things, apply for and obtain institutional review board, or IRB, approval of the proposed investigation. In addition, if the clinical study involves a "significant risk" (as defined by the FDA) to human health, the sponsor of the investigation must also submit and obtain FDA approval of an IDE application and follow applicable IDE regulations. Unless IDE-exempt, nonsignificant risk devices are still subject to certain abbreviated IDE requirements; however, an IDE application is not required if such abbreviated requirements are met. We may not be able to obtain any necessary FDA and/or IRB approval to undertake clinical studies in the United States for future devices we develop and intend to market in the United States. If we do obtain such approvals, the FDA may find that our studies do not comply with the IDE or other regulations governing clinical investigations or the data from any such studies may not support marketing authorization of the investigational device. Moreover, certainty that clinical studies will meet desired endpoints or produce meaningful or useful data and be free of unexpected adverse effects cannot be assured, and such uncertainty could preclude or delay marketing authorization resulting in significant financial costs and reduced revenue.

While we plan to submit IDEs or comparable documents for Revita, we may not be able to file such IDEs or comparable documents on the timeline we expect. For example, we may experience manufacturing delays or other delays. Moreover, we cannot be sure that submission of an IDE or comparable document will result in the FDA or other comparable foreign regulatory authorities allowing further clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate clinical studies. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical studies set forth in an IDE, we

cannot guarantee that such regulatory authorities will not change their requirements in the future. In addition, the FDA may disapprove of our IDE or withdraw approval of a previously-approved IDE if it finds that:

- we have not complied with certain requirements of the IDE regulations, any other applicable regulations or statutes, or any condition of approval imposed by an IRB or the FDA;
- the application or a report contains untrue statements or omits required material information;
- we fail to respond to a request for additional information within the time prescribed by the FDA;
- there is reason to believe that the risks to the human subjects are not outweighed by the anticipated benefits to the subjects or the importance of the knowledge to be gained;
- the informed consent is inadequate;
- the investigation, as proposed, is scientifically unsound;
- there is reason to believe that the device as used is ineffective; or
- it is unreasonable to begin or to continue the investigation due to the way in which the device is used or the inadequacy of:

  (i) the report of prior investigations or the investigational plan;

  (ii) the methods, facilities, and controls used for the manufacturing, processing, packaging, storage, and, where appropriate, installation of the device; or

  (iii) the monitoring and review of the investigation.

Although we would expect to submit a compliant, truthful and complete application, we cannot guarantee that the FDA would approve it. If the FDA were to disapprove our IDE application or propose to withdraw prior approval, we would have the right to request a regulatory hearing. However, we cannot guarantee what the outcome of such a hearing would be. If are required and fail to obtain approval of an IDE, the FDA may prohibit us from conducting our investigation, or place us on a "clinical hold," which could result in significant delay to our clinical studies or prevent us from completing them at all.

We may not be able to file INDs or IND amendments or comparable documents in foreign jurisdictions to commence additional clinical studies on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

While we plan to submit INDs or comparable documents for our Rejuva gene therapy candidate, we may not be able to file such INDs or comparable documents on the timeline we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND or comparable document will result in the FDA or other comparable foreign regulatory authorities allowing further clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate clinical studies. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical studies set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical studies we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs on the timelines we expect or to obtain regulatory approvals for our study may prevent us from completing our clinical studies or commercializing our product candidates on a timely basis, if at all.

Interim, topline and preliminary data from our clinical studies that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical and clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or study. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the topline or preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical and clinical studies. Interim data from clinical studies that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

In addition, the information we choose to publicly disclose regarding a particular study or clinical study is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Our product candidates may cause serious adverse events or undesirable side effects or have other properties which may cause us to suspend or discontinue clinical studies, delay or prevent regulatory approval or certification, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects that may be caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in a more restrictive label than anticipated or the delay or denial of regulatory approval or certification by the FDA or comparable foreign regulatory authorities or notified bodies. Results of our clinical studies could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

If unacceptable side effects or deaths arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted, DSMB or other regulatory authorities could suspend or terminate our clinical studies or the FDA or other regulatory authorities could order us to cease clinical studies or deny approval or certification of our product candidates for any or all targeted indications. Undesirable side effects or deaths in clinical studies with our product candidates may cause the FDA or comparable foreign regulatory authorities to place a clinical hold on the associated clinical studies, to require additional studies, or otherwise to delay or deny approval or certification of our product candidates for any or all targeted indications. Such side effects could also affect patient recruitment or the ability of enrolled patients to complete the study or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical studies and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval or certification and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities or notified bodies may suspend, limit or withdraw approvals or certifications of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities or notified bodies may require additional warnings on the label, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical studies or post-approval studies;
- we may be required to create a risk evaluation and mitigation strategy, or REMS, or similar mitigation plans in the case of our Rejuva gene therapy candidate, which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved or certified, and could seriously harm our business.

In previous clinical studies conducted by third parties involving viral vectors for gene therapy, some patients experienced serious adverse events, including the development of leukemia due to vector-related insertional oncogenesis. If our vectors demonstrate a similar effect, we may be required to halt or delay clinical development of our Rejuva gene therapy candidate or future gene therapy candidates.

A significant risk in any gene therapy product based on viral vectors is that the vector will insert in or near cancer-causing oncogenes leading to uncontrolled clonal proliferation of mature cancer cells in the patient. For example, in 2003, clinical studies using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts in or near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer, often leukemia. Using molecular diagnostic techniques, it was determined that clones from these patients showed retrovirus insertion in proximity to the promoter of the *LMO2* proto-oncogene. Earlier generation retroviruses like the one used in these two studies have been shown to preferentially integrate in regulatory regions of genes that control cell growth.

These well-publicized adverse events led to the development of new viral vectors, such as AAV vectors, which is what we use for our current Rejuva gene therapy candidate, with the goal of potentially improved safety profiles, as well as the requirement of enhanced safety monitoring in gene therapy clinical studies, including routine performance of vector copy number analysis on all production lots to monitor the number of insertion events per cell. Notwithstanding the potential safety improvements of AAV vectors, the risk of insertional oncogenesis remains a significant concern for gene therapy, and we cannot be certain that it will not occur in any of our clinical studies. There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. The FDA has stated that AAV vectors possess characteristics that may pose risks of delayed adverse events. If any such adverse events occur, advancement of our preclinical and clinical studies could be halted or delayed, which would have a material adverse effect on our business and operations.

Although Revita has received Breakthrough Device designation, there can be no guarantee that the designation will benefit the development and regulatory approval process.

Revita has received Breakthrough Device designation from the FDA for the hydrothermal ablation of the duodenal mucosa to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin therapy. Breakthrough Device designation is available to medical devices that meet certain eligibility criteria, including that there is a reasonable expectation that the device will provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, and that the device meets one of the following criteria: (i) the device represents a breakthrough technology, (ii) no approved or cleared alternatives exist, (iii) the device offers significant advantages over existing approved or cleared alternatives, or (iv) the availability of the device is in the best interest of patients. In granting breakthrough device designation to Revita, the FDA found the following: there is a reasonable expectation that Revita will provide for more effective treatment or T2D patients who are inadequately controlled on long-acting insulin therapy; Revita represents a breakthrough technology; Revita, if found to be safe and effective, could offer significant advantages over existing approved or cleared alternatives; and the availability of Revita, if found to be safe and effective, would be in the best interest of patients. Breakthrough Device designation provides certain benefits to device developers, including more interactive and timely communications with FDA staff, use of postmarket data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design, and prioritized review of premarket submissions.

However, we may not experience a faster development process or review, and Breakthrough Device designation has no bearing on whether or not we will obtain approval, as compared to conventional FDA procedures. Breakthrough Device designation does not alter or convey any advantage in the regulatory review and approval standard for medical devices. Further, the FDA may rescind Breakthrough Device designation if it believes that the designation is no longer supported by data from our clinical development program.

If healthcare providers are unable to obtain coverage or adequate reimbursement for procedures performed with our products, if approved, such products will not likely be widely used.

In the United States, the commercial success of Revita and any future products will depend, in part, on the extent to which governmental payors at the federal and state levels, including Medicare and Medicaid, private health insurers and other third-party payors provide coverage for and establish adequate reimbursement levels for procedures utilizing our products, if approved.

Hospitals and other healthcare providers that purchase our product, if approved, for treatment of their patients generally rely on third-party payors to pay for all or part of the costs and fees associated with our products, if approved, as part of a “bundled” rate for the associated procedures. The existence of coverage and adequate reimbursement for our products, if approved, and the procedures performed with them by government and private payors is critical to market acceptance of our existing and future products. Neither hospitals nor physicians are likely to use our product, if approved, and any future products if they do not receive adequate reimbursement for the procedures utilizing such products.

Many private payors currently base their reimbursement policies on the coverage decisions and payment amounts determined by the Centers for Medicare & Medicaid Services, or CMS, which administers the Medicare program. Others may adopt different coverage or reimbursement policies for procedures performed with our products, if approved, while some governmental programs, such as Medicaid, have reimbursement policies that vary from state to state, some of which may not pay for the procedures performed with our products in an adequate amount, if at all. A Medicare national or local coverage decision denying coverage for our products or for procedures using our products could result in private and other third-party payors also denying coverage for our products or procedures using our products. Third-party payors also may deny reimbursement for our products or procedures using our products if they determine that a product used in a procedure was not medically necessary, was not used in accordance with cost-effective treatment methods, as determined by the third-party

payor, or was used for an unapproved use. Unfavorable coverage or reimbursement decisions by government programs or private payors underscore the uncertainty that our product face in the market and could have a material adverse effect on our business.

Many hospitals, clinics and other health care providers in the United States participate in group purchasing organizations, or GPOs, which may incentivize their members to make a relatively large proportion of purchases of medical technology from a limited number of vendors of similar products that have contracted with the GPO to offer discounted prices to the GPO's members. Accordingly, the commercial success of our products may also depend to some extent on our ability to either negotiate favorable purchase contracts with key group purchasing organizations and/or persuade hospitals and clinics to purchase our product "off contract." The healthcare industry in the United States has experienced a trend toward cost containment as government and private payors seek to control healthcare costs by paying service providers lower rates. While we believe that hospitals will be able to obtain coverage for procedures using our products, the level of payment available to them for such procedures may change over time. State and federal healthcare programs, such as Medicare and Medicaid, closely regulate provider payment levels and have sought to contain, and sometimes reduce, payment levels. Private payors frequently follow government payment policies and are likewise interested in controlling increases in the cost of medical care. In addition, some payors are adopting pay-for-performance programs that differentiate payments to healthcare providers based on the achievement of documented quality-of-care metrics, cost efficiencies, or patient outcomes. These programs are intended to provide incentives to providers to deliver the same or better results while consuming fewer resources. Because of these programs, and related payor efforts to reduce payment levels, hospitals and other providers are seeking ways to reduce their costs, including the amounts they pay to medical device manufacturers. We may not be able to sell our product profitably if third-party payors deny or discontinue coverage or reduce their levels of payment below that which we project, or if our production costs increase at a greater rate than payment levels. Adverse changes in payment rates by payors to hospitals could adversely affect our ability to market, sell our products, and negatively affect our financial performance.

In international markets, medical device regulatory requirements and healthcare payment systems vary significantly from country to country, and many countries have instituted price ceilings on specific product lines. We cannot assure you that our products will be considered cost-effective by international third-party payors, that reimbursement will be available or, if available, that the third-party payors' reimbursement policies will not adversely affect our ability to sell our product profitably. Any failure to receive regulatory or reimbursement approvals would negatively affect market acceptance of our products in any international markets in which those approvals are being sought.

Additional time may be required to develop and obtain regulatory approval or certification for our Rejuva gene therapy candidate because we expect it to be regulated as a combination product.

We expect our Rejuva gene therapy candidate to require the development of a drug delivery device, such that the gene therapy candidate and drug delivery device may be regulated as a biologic-device combination product that requires coordination within the FDA and similar foreign regulatory agencies and notified bodies for review of its device and biologic components. Although the FDA and similar foreign regulatory agencies and notified bodies have systems in place for the review and approval or certification of combination products such as our Rejuva gene therapy candidate, we may experience delays in the development, approval or certification, and commercialization of our Rejuva gene therapy candidate due to regulatory timing constraints and uncertainties in the product development and approval or certification process.

Obtaining and maintaining regulatory approval or certification of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval or certification of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval, clearance, or certification of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval, clearance, or

certification in any other jurisdiction, while a failure to obtain or delay in obtaining regulatory approval, clearance, or certification in one jurisdiction may have a negative effect on the regulatory approval, clearance, or certification process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval or certification procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical or clinical studies as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities or notified bodies in other jurisdictions. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval.

We may also submit marketing applications or certifications in other countries. Regulatory authorities and notified bodies in jurisdictions outside of the United States have requirements for approval and certification of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals or certifications and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products, if approved, in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals and/or certifications, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we receive regulatory approval or certification of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

The regulations to which we are subject are complex and have become more stringent over time. Regulatory changes could result in restrictions on our ability to continue or expand our operations, higher than anticipated costs, or lower than anticipated sales. Even after we have obtained the proper approval or certification to market a device, biological product, or combination product, we will have ongoing responsibilities under FDA regulations and applicable foreign laws and regulations.

Any regulatory approvals or certifications that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority or notified body approves or certifies our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practice requirements, or cGMPs, or similar foreign requirements, good clinical practice requirements, or GCPs, for any clinical studies that we conduct post-approval, and applicable product tracking and tracing requirements for certain drug and biological products. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP or similar foreign requirements and adherence to commitments made in any marketing application and previous responses to inspectional observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. In addition, the FDA and foreign regulatory authorities could require us to conduct another study to obtain additional safety or biomarker information.

Further, we will be required to comply with FDA and other regulatory authorities' promotion and advertising rules, which include, among others, restrictions on promoting products for uses or in patient populations that are not described in the product's approved uses (known as "off-label use"), limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet and social media. Although the FDA and other regulatory authorities do not regulate a physician's choice

of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance or certification has not been issued. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party suppliers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS or similar program for our gene therapy candidates, if approved.

Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or product recalls;
- fines, untitled letters, warning letters or holds on clinical studies;
- refusal by the FDA or similar foreign authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals or similar approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

FDA and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval or certification of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval or certification that we may have obtained and we may not achieve or sustain profitability.

For instance, in April 2014 the EU adopted the Clinical Trials Regulation, or CTR, which will become applicable on January 31, 2022. The CTR will be directly applicable in all EU member states, repealing the current Clinical Trials Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new CTR becomes applicable. The extent to which ongoing clinical trials will be governed by the CTR will depend on the duration of the individual clinical trial from January 31, 2022 onward. If an ongoing clinical trial continues for more than three years from January 31, 2022 the CTR will begin to apply to the clinical trial as of January 31, 2025. The CTR harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which will notably contain a centralized EU portal and database.

In addition, the EU landscape concerning medical devices recently evolved. On May 25, 2017, the Medical Devices Regulation entered into force, which repeals and replaces the EU MDD and the Active Implantable MDD. Unlike directives, which must be implemented into the national laws of the EU member states, regulations are directly applicable (i.e., without the need for adoption of EU member state laws implementing them) in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member States.

The Medical Devices Regulation, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU and EEA for medical devices and ensure a high

level of safety and health while supporting innovation. The Medical Devices Regulation became effective on May 26, 2021. The new regulation among other things:

- strengthens the rules on placing devices on the market (e.g. reclassification of certain devices and wider scope than the EU MDD) and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow up of the quality, performance and safety of devices placed on the market;
- imposes an obligation to identify a responsible person who is ultimately responsible for all aspects of compliance with the requirements of the new regulation;
- improves the traceability of medical devices throughout the supply chain to the end user or patient through the introduction of a unique identification number, to increase the ability of manufacturers and regulatory authorities to trace specific devices through the supply chain and to facilitate the prompt and efficient recall of medical devices that have been found to present a safety risk;
- sets up a central database (EUDAMED) to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU and EEA; and
- strengthens the rules for the assessment of certain high risk devices, such as implants, which may have to undergo a clinical evaluation consultation procedure by experts before they are placed on the market.

These modifications may have an effect on the way we intend to develop our business in the EU and EEA. For example, as a result of the transition towards the new regime, notified body review times have lengthened, and product introductions could be delayed or canceled, which could adversely affect our ability to grow our business.

We expect our Rejuva gene therapy candidate will be, and future gene therapy candidates may be, regulated as biological products, or biological product-device combination products, and therefore may be subject to competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Affordable Care Act to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when processes intended to implement BPCIA may be fully adopted by the FDA, any of these processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the product candidates we develop that is approved in the United States as a biological product under a BLA, if any, should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In addition, the approval of a biologic product biosimilar to one of our product candidates could have a material adverse impact on our business as it may be significantly less costly to bring to market and may be priced significantly lower than our products.

Disruptions at the FDA and other government agencies or notified bodies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, cleared or approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA, similar foreign regulatory authorities and notified bodies to review and authorize or certify new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the European Medicines Agency, following its relocation to Amsterdam and corresponding staff changes, may also slow the time necessary for new products or modifications to cleared or approved products to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020 the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

For instance in the EU, notified bodies must be officially designated to certify products and services in accordance with the Medical Devices Regulation. While several notified bodies have been designated the COVID-19 pandemic has significantly slowed down their designation process and the current designated notified bodies are facing a large amount of requests with the new regulation and notified body review times have lengthened. This situation could impact our ability to grow our business in the EU and EEA.

A recall of our products, if approved, either voluntarily or at the direction of the FDA or another governmental authority, or the discovery of serious safety issues with our products, could have a significant adverse impact on us.

The FDA and similar foreign governmental authorities have the authority to require the recall of commercialized medical devices in the event of material deficiencies or defects in design or manufacture or in the event that a product poses an unacceptable risk to health. Manufacturers may, under their own initiative, recall a product if any material deficiency in a device is found. A government-mandated or voluntary recall by us or one of our distributors could occur as a result of an unacceptable risk to health, component failures, manufacturing errors, design or labeling defects or other deficiencies and issues. Recalls of any of our products

would divert managerial and financial resources and have an adverse effect on our reputation, results of operations and financial condition, which could impair our ability to produce our products in a cost-effective and timely manner in order to meet our customers' demands. We may also be required to bear other costs or take other actions that may have a negative impact on our future sales and our ability to generate profits.

Further, under the FDA's medical device reporting regulations, we are required to report to the FDA any incident in which a commercialized medical device product may have caused or contributed to a death or serious injury or in which our product malfunctioned and, if the malfunction were to recur, would likely cause or contribute to death or serious injury. Repeated product malfunctions may result in a voluntary or involuntary product recall, which could divert managerial and financial resources, impair our ability to manufacture our products in a cost-effective and timely manner and have an adverse effect on our reputation, results of operations and financial condition.

In the EEA, we must comply with the EU medical device vigilance system. Under this system, serious incidents and Field Safety Corrective Actions, or FSCAs must be reported to the relevant authorities of the EEA. These reports will have to be submitted through EUDAMED—once functional—and aim to ensure that, in addition to reporting to the relevant authorities of the EU member states, other actors such as the economic operators in the supply chain will also be informed. Until EUDAMED is fully functional, the corresponding provisions of the MDD continue to apply. FSCAs must be communicated by the manufacturer or its legal representative to its customers and/or to the end users of the device through Field Safety Notices, or FSNs. For similar serious incidents that occur with the same device or device type and for which the root cause has been identified or a FSCA implemented or where the incidents are common and well documented, manufacturers may provide periodic summary reports instead of individual serious incident reports.

Any adverse event involving our products, whether in the United States or abroad, could result in future voluntary corrective actions, such as recalls or customer notifications, or agency action, such as inspection, mandatory recall or other enforcement action. Any corrective action, whether voluntary or involuntary, as well as defending ourselves in a lawsuit, will require the dedication of our time and capital, distract management from operating our business and may harm our reputation and financial results.

If we obtain approval or certification of any of our product candidates, we may be subject to enforcement action if we engage in the off-label promotion of our products.

If we obtain approval or certification for any product candidates, our promotional materials and training methods must comply with FDA and other applicable laws and regulations, including the prohibition on the promotion of off-label use. Physicians may use our products off-label, as the FDA does not restrict or regulate a physician's choice of treatment within the practice of medicine. For example, we are pursuing market authorization for Revita to improve glycemic control and eliminate insulin needs in T2D patients inadequately controlled on long-acting insulin, but physicians may decide to use Revita for other, non-approved, T2D patient populations. If the FDA determines that our promotional materials or training constitutes promotion of an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine and criminal penalties. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our promotional or training materials to constitute promotion of an unapproved use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. In that event, our reputation could be damaged and adoption of the products would be impaired. Although our policy is to refrain from statements that could be considered off-label promotion of our products, the FDA or another regulatory agency could disagree and conclude that we have engaged in off-label promotion. In addition, the off-label use of our products may increase the risk of injury to patients, and, in turn, the risk of product liability claims. Product liability claims are expensive to defend and could divert our management's attention, result in substantial damage awards against us and harm our reputation.

Risks Related to Our Business and Strategy

We are substantially dependent on the success of our lead product candidate, Revita. If we are unable to obtain marketing approval or certification for and commercialize any of our current or future product candidates in a timely manner, our business will be harmed.

Our future success is dependent on our ability to timely advance and complete clinical studies, obtain marketing approval or certification for and successfully commercialize Revita. In 2016, Revita was CE marked under the EU Medical Devices Directive. The certificate was renewed on March 8, 2021. However, we do not currently market this product in the EU or UK. We are investing significant efforts and financial resources in the research and development of Revita as well as our Rejuva gene therapy candidate. We are currently conducting a pivotal clinical study of Revita for T2D patients that are inadequately controlled on metformin, up to two additional ADAs, and long-acting insulin. Revita will require additional clinical development, evaluation of clinical manufacturing activities, marketing approval from government regulators, substantial investment and significant marketing efforts before we can generate any revenues from product sales. We are not permitted to market or promote Revita or any other product candidate, before we receive marketing approval or certification from the FDA or comparable foreign regulatory authorities or notified bodies, and we may never receive such marketing approvals or certifications.

The success of Revita will depend on several factors, including the following:

- the successful and timely completion of our ongoing or planned clinical studies, including any delays arising out of the COVID-19 pandemic;
- the initiation and successful patient enrollment and completion of additional clinical studies on a timely basis;
- maintaining and establishing relationships with CROs and clinical sites for clinical development, both in the United States and internationally;
- the frequency and severity of adverse events in the clinical studies;
- the efficacy, safety and tolerability profiles that are satisfactory to the FDA or any comparable foreign regulatory authority or notified bodies for marketing approval or certification;
- the timely receipt of marketing approvals or certifications from applicable regulatory authorities or notified bodies;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- maintaining our manufacturing facility and certain regulatory requirements thereof;
- the maintenance of existing or the establishment of new supply arrangements with third-party drug product suppliers and manufacturers for clinical development;
- the maintenance of existing, or the establishment of new, scaled production arrangements with third-party manufacturers to obtain finished products that are appropriate for commercial sale of our product candidates, if approved or certified;
- the protection of our rights in our intellectual property portfolio;
- the successful launch of commercial sales following any marketing approval or certification;

- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize Revita, which would materially harm our business. If we do not receive marketing approvals or certification under the Medical Devices Regulation for Revita, we may not be able to continue our operations.

Our long-term prospects depend in part upon discovering, developing and commercializing product candidates, which may fail in development or suffer delays that adversely affect their commercial viability. We intend to identify and develop novel product candidates, which makes it difficult to predict the time, cost and potential success of our current product candidates, and other product candidates we may develop in the future.

Our future results of operations are dependent on our ability to successfully discover, develop, obtain regulatory approval or certification for and commercialize product candidates beyond those we currently have in preclinical studies and clinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical or early clinical studies of a product candidate may not be predictive of the results that will be obtained in later stage clinical studies of the product candidate.

The success of the product candidates we have or may develop will depend on many factors, including the following:

- the success of our research methodology in identifying potential indications or product candidates;
- generating sufficient data to support the initiation or continuation of clinical studies;
- obtaining regulatory permission to initiate clinical studies;
- contracting with the necessary parties to conduct clinical studies;
- successful enrollment of patients in, and the completion of, clinical studies on a timely basis;
- the timely manufacture of sufficient quantities of the applicable product candidate for use in clinical studies;
- the possible occurrence of adverse events in our clinical studies; and
- any potential interruptions or delays resulting from factors related to the COVID-19 pandemic or any future public health crises, including epidemics and pandemics.

In addition, our strategy includes identifying, developing and commercializing our Rejuva gene therapy candidate by using an AAV vector for endoscopic delivery of transgenes, such as GLP-1 receptor analog, to the pancreas to enable long-term remission of T2D by potentially restoring insulin production in patients with

advanced disease. Our future success depends on the successful development of our Rejuva gene therapy platform. To date, very few products that utilize gene transfer have been approved in the United States or Europe and no gene therapy products that utilize an endoscopic method of administration have been approved. In addition, there have been a limited number of clinical studies of gene transduction technologies as compared to other, more conventional forms of therapy.

Although several AAV vectors have been tested in numerous clinical studies and are currently used in FDA-approved products, we cannot be certain that our Rejuva gene therapy candidate will successfully complete preclinical and clinical studies, or that it will not cause significant adverse events or toxicities. We also cannot be certain that we will be able to avoid triggering toxicities in our future preclinical or clinical studies or that our endoscopic method of administration will not cause unforeseen side effects or other challenges. Any such results could impact our ability to develop a product candidate, including our ability to enroll patients in our clinical studies. As a result of these factors, it is more difficult for us to predict the time and cost of our Rejuva gene therapy candidate's development, and we cannot predict whether the application of our approach to gene therapy, or any similar or competitive programs, will result in the identification, development, and regulatory approval of Rejuva, or that other gene therapy programs will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to our Rejuva gene therapy candidate or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays and challenges in achieving sustainable, reproducible, and scalable production. Any of these factors may prevent us from completing our preclinical or clinical studies or commercializing any gene therapy candidates we may develop on a timely or profitable basis, if at all.

Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this "Risk Factors" section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval or certification of, commercialize or generate significant revenue from our other product candidates.

We may not be able to gain the support of leading hospitals and key thought leaders, or to publish the results of our clinical studies in peer-reviewed journals, which may make it difficult to establish the Revita DMR Procedure and/or our Rejuva gene therapy candidate as a standard of care, if approved, and may limit our revenue growth and ability to achieve profitability.

Our strategy includes developing relationships with leading hospitals and key thought leaders in the industry. If these hospitals and key thought leaders determine that the Revita DMR Procedure and/or our Rejuva gene therapy candidate is not clinically effective, or that alternative technologies or products are more effective, or if we encounter difficulty promoting adoption of or establishing the Revita DMR Procedure and/or our Rejuva gene therapy candidate as a standard of care, once approved or certified, our revenue growth and our ability to achieve profitability could be significantly limited.

We believe that the successful completion of our clinical studies of the Revita DMR Procedure and our Rejuva gene therapy candidate, publication of scientific and medical results in peer-reviewed journals, and presentation of data at leading conferences are critical to the broad adoption of the Revita DMR Procedure and our Rejuva gene therapy candidate. Publication in leading medical journals is subject to a peer-review process, and peer reviewers may not consider the results of studies involving the Revita DMR Procedure and/or our Rejuva gene therapy candidate sufficiently novel or worthy of publication.

We have not yet studied the ability of Revita to be used in repeated procedures and we are uncertain as to whether patients will need additional procedures in the future. If we are unable to demonstrate the safety and improved glycemic effects of Revita for repeat use, it could have a material adverse effect on the on the clinical utility and commercial adoption of the device.

We have not yet studied the ability of Revita to be used in repeat procedures and we are uncertain as to whether patients will need additional procedures in the future. Although, in a long-term follow-up study of the PP population in our Revita-1 study, we observed a statistically significant mean HbA1c reduction of 1.0% (n=27) at 24 months in patients who underwent the Revita DMR Procedure, in combination with at least one ongoing OAD and lifestyle counseling, we cannot be certain that patients will not need additional procedures in the future. To the extent that additional procedures are needed, it could have a material adverse effect on the clinical utility and commercial adoption of Revita. In addition, if we are unable to demonstrate the safety of Revita for repeat use, if necessary, it could have a material adverse effect on the clinical utility and commercial adoption of Revita because providers, referring physicians, payors and patients may not find the product to be a compelling treatment option for T2D patients. To the extent any of the aforementioned groups do not accept Revita as a compelling treatment option for T2D patients, it could significantly harm our business, financial condition and prospects.

We have never obtained marketing approval for a product candidate in the United States and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any product candidate in the United States.

We have never obtained marketing approval for a product candidate in the United States. It is possible that the FDA may refuse to accept for substantive review any PMAs, BLAs or similar applications that we submit for our product candidates or may conclude after review of our data that our applications are insufficient to obtain marketing approval of our product candidates. We believe our proposed approach of treating T2D through the Revita DMR Procedure and our Rejuva gene therapy candidate is novel and, as a result, the process for, and the outcome of, our efforts to seek FDA approval is especially uncertain. If the FDA does not accept or approve our PMAs or BLAs for our product candidates, it may require that we conduct additional clinical, preclinical, or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any PMA or BLA that we submit may be delayed or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve our PMAs or BLAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues, and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

If we are unable to obtain a billing code from the U.S. Department of Health and Human Services so that procedures using Revita, if approved, are covered under Medicare and Medicaid, this could have a negative impact on our intended sales and would have a material adverse effect on our business, financial condition and operating results.

We plan to submit an application to the U.S. Department of Health and Human Services for a billing code so that procedures using Revita, if approved, are covered under Medicare and Medicaid. However, there can be no assurance that our application will be successful, or that we will be able to obtain a code in a timely manner. In the event that we do not obtain a billing code for Revita, our customers may be unable to obtain reimbursement to cover the cost of their purchases under private or government-sponsored insurance plans, which could have a negative impact on our sales and have a material adverse effect on our business, financial condition and operating results. In addition, Medicare and its administrative contractors as well as other insurers

must find that Revita meets their medical necessity requirements for the treatment of patients with T2D on long-acting insulin or they will not pay for the treatment. In addition, there is a risk that the payment amount for Revita could be too low or too high to incentivize customer adoption.

If Revita, our Rejuva gene therapy candidate or any of our other future product candidates is approved or certified and fail to achieve and sustain sufficient market acceptance, we will not generate expected revenue and our business may be harmed.

Commercialization of our Revita DMR System, our Rejuva gene therapy candidate and any of our other future product candidates in the United States and other jurisdictions in which we intend to pursue marketing approval or certification for such product candidates is a key element of our strategy. To be commercially successful, we must establish through clinical studies and convince physicians, hospitals and other healthcare providers, as well as potential patients, that the Revita DMR Procedure and our Rejuva gene therapy candidate are superior and attractive alternatives to currently available treatment options. Acceptance of our Rejuva gene therapy candidate and the Revita DMR Procedure depends on establishing their safety and effectiveness, including the Revita DMR Procedure's durability in treating T2D, and educating our target audience about their distinct characteristics, potential benefits, safety and ease-of-use. If we are not successful in establishing safety, effectiveness and ease of use, and conveying that our product candidates, if approved or certified, or the procedures and treatment they enable, provide superior results compared to existing technologies, practices and/or therapies, or that these product candidates improve patient outcomes, we may experience reluctance or refusal on the part of physicians, hospitals and other healthcare providers to accept and order, and third-party payors to pay for the treatment or procedures performed with, our product candidates, or patients may elect not to undergo the Revita DMR Procedure or take our Rejuva gene therapy candidate.

We believe that physicians, hospital and other healthcare providers will not widely accept our product candidates unless they are able to determine that our product candidates provide a benefit to patients and are a superior alternative to currently available interventions and easily integrated into their current endoscopy suite. Physicians, hospitals and other healthcare providers may be hesitant to change their medical treatment practices for the following reasons, among others:

- comfort and experience with current treatment regimens;
- long-standing relationships with competitors and distributors that sell other products and such parties' negative selling efforts;
- perceived liability risks generally associated with the use of new products and procedures;
- lack or perceived lack of long-term clinical data relating to safety or effectiveness, including durable effectiveness;
- difficulty in using Revita;
- higher cost or perceived higher cost of our product candidate compared to currently available treatments; and
- the additional time commitment that may be required for training.

These hurdles may make it difficult to demonstrate to physicians, hospitals and other healthcare providers that the Revita DMR Procedure and our Rejuva gene therapy candidate are an appropriate option for treating metabolic diseases, such as T2D, may be superior to available treatments and may be more cost-effective than alternative technologies. Furthermore, we may encounter significant difficulty in gaining inclusion in metabolic disease treatment guidelines and gaining broad market acceptance by healthcare providers, third-party payors and patients for our products, if approved, or procedures in which our products are used.

In addition, patient satisfaction with the Revita DMR Procedure and our Rejuva gene therapy candidate will be an important factor in providers' decisions to use our products. The success of any particular procedure using our products, and a patient's satisfaction with the procedure, is dependent on the technique and execution of the procedure by the endoscopist. Even if our products are manufactured exactly to specification, there is a risk that the endoscopist may not perform the procedure to specifications, leading to patient dissatisfaction with the procedure. If patients do not have a good outcome following procedures conducted using our products, providers' views of our products may be negatively impacted.

If we fail to successfully commercialize our products, if approved or certified, we may never receive a return on the significant investments in product development, sales and marketing, regulatory, manufacturing and quality assurance we have made, or further investments we intend to make, and we may fail to generate revenue or gain economies of scale from such investments.

Our future growth depends on physician awareness and adoption of the Revita DMR Procedure.

We intend to focus our sales, marketing and training efforts on diabetologists, gastroenterologists and interventional endoscopists. However, the initial point of contact for many patients suffering from T2D may be primary care physicians, or PCPs, or other referring medical professionals, such as nurse practitioners or physician assistants, who commonly see patients who have, or who are at risk of developing, T2D. We believe that education of PCPs, and other medical professionals caring for patients with metabolic diseases, about the clinical merits and patient benefits of the Revita DMR Procedure and our Rejuva gene therapy candidate is an important element of the adoption and market acceptance of our product candidates. If we fail to educate PCPs and other medical professionals, or if we educate them but they disagree with the clinical merits, patient benefits and ease-of-use of the DMR procedure using Revita and/or our Rejuva gene therapy candidate, or do not modify their current referral pattern to refer T2D patients to diabetologists, gastroenterologists and interventional endoscopists to perform the DMR procedure using Revita, our ability to achieve our projected revenues may be impaired.

The training required for endoscopists to use Revita could reduce the market acceptance of our products.

As with any new method or technique, endoscopists must undergo a training program before they are qualified to perform DMR procedure using Revita and administer our Rejuva gene therapy candidate. Endoscopists may not achieve the technical competency necessary to perform the procedure. We could also experience difficulty in meeting expected levels of endoscopists' completing our training program. This could happen due to there being less demand than expected, the length of time necessary to train each endoscopist being longer than we anticipate and/or the capacity of our future sales representatives to train endoscopists being lower than expected.

We have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators.

We have never commercialized a product candidate, and we currently have no sales force, marketing or distribution capabilities. We will have to develop our own sales, marketing and supply organization or outsource these activities to a third party to commercialize our products. If we decide to license our product candidate to others, we may need to rely on the marketing assistance and guidance of those collaborators.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may not generate revenues from them or be able to reach or sustain profitability.

The medical device, diabetes management and biopharmaceutical markets are highly competitive. We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.

If our device product candidates receive marketing authorization or are cleared, approved or certified by regulatory authorities or notified bodies, when we commercialize our products we will compete with commercial medical device and diabetes management companies that offer a wider variety of products, services and procedures within the diabetic care categories. Some of these product offerings include: lifestyle and diet services, pharmaceuticals, and bariatric surgeries, in particular gastric bypass surgeries. Most of our expected competitors are either publicly traded or are divisions of publicly traded companies and have a number of competitive advantages over us, including:

- greater name and brand recognition, and financial and human-capital resources;
- longer commercial histories and better-established, broader operations and product lines and pipelines;
- larger sales forces and more established distribution networks;
- greater experience in conducting research and development, manufacturing, clinical studies, preparing regulatory submissions and obtaining regulatory clearance, approval or certification for product candidates;
- substantial intellectual property portfolios;
- larger and better-established customer bases and more extensive relationships with physicians, including diabetologists and endoscopists, providing them with more opportunities to interact with stakeholders involved in purchasing decisions; and
- better-established, larger-scale and lower-cost manufacturing capabilities and supplier relationships.

We believe that the principal competitive factors in our target markets include:

- safety and impact of products and procedures on the health of the patient;
- acceptance by diabetologists, endoscopists, endocrinologists, PCPs and other healthcare providers;
- reputation among physicians, hospitals and other healthcare providers;
- effectiveness, ease-of-use and reliability of the Revita DMR Procedure;
- capital and per-procedure economics of the DMR procedure using Revita;
- capital and per-treatment economics of our Rejuva gene therapy candidate;
- ability to implement a consumables-based model for product candidates;
- innovation in product candidate offerings;
- effective manufacturing, sales, marketing and distribution channels; and
- technical superiority of the Revita DMR Procedure in comparison to current treatment options.

We cannot assure you that we will effectively compete or that we will be successful in the face of increasing competition from existing and new products and technologies introduced by competitors, including pharmaceutical therapies to treat the same metabolic diseases as those targeted by our product candidates. We cannot assure you that our future competitors do not have or will not develop products or technologies that enable them to produce competitive products with greater capabilities or at lower costs than our product candidates. Any failure to compete effectively could materially and adversely affect our business, financial condition and operating results.

In addition, the biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize, such as our Rejuva gene therapy candidate, will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates.

In particular, there is intense competition in the field of gene therapy we are pursuing. We have competitors both in the United States and internationally, including major multinational biopharmaceutical companies, established biotechnology companies, specialty biopharmaceutical companies, emerging and start-up companies, universities and other research institutions. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical study sites, enrolling subjects for clinical studies and in identifying and in-licensing new product candidates.

We have chosen to initially address a well-validated biochemical target, and therefore expect to face competition from existing products and products in development for each of our product candidates. There are a large number of companies developing or marketing gene therapies, including many major pharmaceutical and biotechnology companies. Many of these current and potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources and commercial expertise than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established biopharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may succeed in obtaining approval from the FDA or other comparable foreign regulatory authorities or in discovering, developing and commercializing products in our field before we do.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain marketing approval from the FDA or other comparable foreign regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete,

less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

We may not be able to develop new product candidates or enhance the capabilities of our existing product candidates to keep pace with our industry's rapidly changing technology and customer requirements, which could have a material adverse impact on our revenue, results of operations and business.

Our industry is characterized by rapid technological changes, frequent new product introductions and enhancements and evolving industry standards. Our success depends on our ability to develop new product candidates and applications for our technology in new markets that develop as a result of technological and scientific advances, while improving the performance and cost-effectiveness of our existing product candidates. New technologies, techniques or products could emerge that might offer better combinations of price and performance than the products and systems that we plan to sell. Existing markets for our intended product candidates are characterized by rapid technological change and innovation. It is critical to our success that we anticipate changes in technology and customer requirements and physician, hospital and healthcare provider practices and successfully introduce new, enhanced and competitive technologies to meet our prospective customers' needs on a timely and cost-effective basis. At the same time, however, we must carefully manage our introduction of new product candidates. If potential customers believe that such product candidates will offer enhanced features or be sold for a more attractive price, they may delay purchases until such product candidates are available. We may also have excess or obsolete inventory of older products as we transition to new product candidates, and we have no experience in managing product transitions. If we do not successfully innovate and introduce new technology into our anticipated product lines or manage the transitions of our technology to new product offerings, our revenue, results of operations and business will be adversely impacted.

Competitors may be able to respond more quickly and effectively than we can to new or changing opportunities, technologies, standards or customer requirements. We anticipate that we will face strong competition in the future as expected competitors develop new or improved products and as new companies enter the market with new technologies.

If the market opportunity for any product candidate that we develop is smaller than we believe, our revenue may be adversely affected and our business may suffer.

Our projections of addressable patient populations that may benefit from treatment with our product candidates are based on our estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, our internal estimates are based in large part on current patterns of treatment selection by diabetologists. Additionally, the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates prove to be inaccurate, the market opportunity for any product candidate that we develop could be significantly diminished and have an adverse material impact on our business.

If the quality of our product candidates does not meet the expectations of diabetologists, gastroenterologists, interventional endoscopists, endocrinologists, PCPs or other referring physicians, or patients, then our brand and reputation could suffer and our business could be adversely impacted.

In the course of conducting our business, we must adequately address quality issues that may arise with our product candidates, as well as defects in third-party components included in our product candidates. Although we have established internal procedures to detect and address quality issues, there can be no assurance that we will be able to eliminate or mitigate risks that may arise from these issues. If the quality of our product candidates does not meet the expectations of diabetologists, gastroenterologists, interventional endoscopists, endocrinologists, PCPs or other referring physicians, or patients, then our brand and reputation could suffer, and our business could be adversely impacted.

Our sales cycle will be lengthy and variable, which makes it difficult for us to forecast revenue and other operating results.

If Revita is approved, we expect that our sales process will involve numerous interactions with multiple individuals within an organization and will often include in-depth analysis by potential customers of our products, performance of proof-of-concept studies, preparation of extensive documentation and a lengthy review process. As a result of these factors and the budget cycles of our potential customers, the time from initial contact with a customer to our receipt of a purchase order will vary significantly and could be up to 12 months or longer. Given the length and uncertainty of our anticipated sales cycle, we likely will experience fluctuations in our product sales on a period-to-period basis. Expected revenue streams are highly dependent on adoption of our consumables-based business model, and we cannot assure you that our potential clients will follow a consistent purchasing pattern. Moreover, it is difficult for us to forecast our revenue from product candidates that are not yet approved for commercialization, as such revenue is dependent upon our ability to establish, and then convince the medical community and third-party payors of, the clinical utility and economic benefits of our product candidates.

Third-party payors may choose not to cover the DMR procedure using Revita or they may require extensive and/or independently performed clinical studies prior to covering or maintaining coverage of the DMR procedure using Revita.

Our success depends on the medical and third-party payor communities' acceptance of our product candidates as tools and/or therapies that are useful to diabetologists, gastroenterologists and interventional endoscopists in treating patients with T2D and other metabolic diseases. The safety and effectiveness of the Revita DMR Procedure and our Rejuva gene therapy candidate have not been established, and we cannot assure you that any data that we or others generate will be consistent with the preclinical and clinical studies we have completed, or those we intend to complete. Even if our clinical studies demonstrate safety and effectiveness sufficient to gain regulatory approval for Revita or our Rejuva gene therapy candidate, certain diabetologists, gastroenterologists, interventional endoscopists, hospitals, ambulatory surgery centers and third-party payors may not find data from our clinical studies compelling or may prefer to see longer-term effectiveness data before adopting or covering the DMR procedure using Revita and/or our Rejuva gene therapy candidate. If providers do not adopt or third-party payors do not provide coverage for the DMR procedure using Revita and/or our Rejuva gene therapy candidate, our business will be materially and adversely affected.

We depend on our information technology systems, and any failure of these systems could harm our business.

We depend on information technology systems for significant elements of our operations, including the storage of data and retrieval of critical business information. We have installed, and expect to expand, a number of enterprise software systems that affect a broad range of business processes and functional areas, including systems handling human resources, financial controls and reporting, contract management, regulatory compliance and other infrastructure operations. These information technology systems may support a variety of functions, including storage of clinical data, laboratory operations, test validation, quality control, customer service support, billing and reimbursement, research and development activities and general administrative activities.

Information technology systems are vulnerable to damage from a variety of sources, including network failures, malicious or accidental human acts and natural disasters. Despite network security and back-up measures, some of our servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Failures or significant downtime of our information technology systems or those used by our third-party service providers could prevent us from conducting our general business operations. Any disruption or loss of information technology systems on which critical aspects of our operations depend could have an adverse effect on our business. Further, we store highly confidential information on our information technology systems, including information related to clinical data, product designs and plans to create new

products. If our systems are compromised by a physical or electronic break-in, computer virus or other malicious or accidental human action, our confidential information could be compromised, stolen or destroyed.

The COVID-19 pandemic and potential future pandemics could continue to adversely impact our business, including our anticipated clinical studies, supply chain and business development activities.

In December 2019, SARS-CoV-2, a novel strain of coronavirus that causes COVID-19, was first reported in Wuhan, China and has since become a global pandemic. The President of the United States declared the COVID-19 pandemic a national emergency and many states and municipalities in the United States have announced aggressive actions to reduce the spread of the disease, including limiting non-essential gatherings of people, ceasing all non-essential travel, ordering certain businesses and government agencies to cease non-essential operations at physical locations and issuing "shelter-in-place" orders which direct individuals to shelter at their places of residence (subject to limited exceptions). We may experience limitations on employee resources in the future, including because of sickness of employees or their families. The effects of government actions and our own policies and those of third parties to reduce the spread of COVID-19 may negatively impact productivity and slow down or delay our future clinical studies, preclinical studies and research and development activities, and may cause disruptions to our supply chain and impair our ability to execute our business development strategy. For example, our U.S. pilot study was prematurely ended due to the COVID-19 pandemic and we have experienced delays in enrollment in other clinical studies due to the COVID-19 pandemic. In addition, we were forced to delay our commercial launch efforts in the United Kingdom due to reduced patient access to hospitals and clinics. In the event that government authorities were to enhance current restrictions, our employees who currently are not telecommuting may no longer be able to access our facilities, and our operations may be further limited or curtailed.

As COVID-19 continues to spread and evolve, we may experience ongoing disruptions that could severely impact our business, preclinical and clinical studies, including:

- interruption or delays in our operations, which may impact our ability to conduct and produce preclinical results required for submission of an IND, IDE or similar foreign applications;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical studies;
- delays or difficulties in enrolling patients in our clinical studies;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical studies, including interruption in global shipping that may affect the transport of clinical study materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical studies are conducted, which may result in unexpected costs, or to discontinue the clinical studies altogether;
- diversion of healthcare resources away from the conduct of clinical studies, including the diversion of hospitals serving as our clinical study sites and hospital staff supporting the conduct of our clinical studies;
- interruption of key clinical study activities, such as clinical study site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical study patient visits and study procedures, the occurrence of which could affect the integrity of clinical study data;

- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- risk that participants enrolled in our clinical studies will acquire COVID-19 while the clinical study is ongoing, which could impact the results of the clinical study, including by increasing the number of observed adverse events; and
- refusal of the FDA or comparable foreign regulatory agencies to accept data from clinical studies in affected geographies.

These and other disruptions in our operations and the global economy could negatively impact our business, results of operations and financial condition.

Our future clinical studies may be affected by the COVID-19 pandemic or any future pandemic. For example, some clinical study sites have slowed down or stopped further enrollment of new patients in clinical studies, denied access to site monitors and otherwise curtailed certain operations. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted. Our planned clinical studies may also be impacted by interruptions or delays in the operations of the FDA and comparable foreign regulatory agencies. We and our CROs will act in accordance with the guidance issued by the FDA and comparable foreign regulatory agencies in our future clinical studies to ensure the monitoring and safety of patients and minimize risks to study integrity during the COVID-19 pandemic. This may have unforeseen effects on the enrollment, progress and completion of these studies and the findings. For example, since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and one of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. These events could also increase the cost of completing our clinical studies and negatively impact the integrity, reliability or robustness of the data from our clinical studies.

In addition, quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities upon which we may rely in the future, or the availability or cost of materials, which could disrupt the supply chain for our product candidates. To the extent our future suppliers and service providers are unable to comply with their obligations under our future agreements with them or they are otherwise unable to deliver or are delayed in delivering goods and services to us due to the COVID-19 pandemic, our future ability to continue meeting clinical supply demand for our product candidates or otherwise advancing development of our product candidates may become impaired.

The spread of COVID-19 and actions taken to reduce its spread may also materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, there could be a significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity and financial position. In addition, the trading prices for other medical device and pharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms.

COVID-19 and actions taken to reduce its spread continue to rapidly evolve. The extent to which COVID-19 may impede the development of our product candidates, reduce the productivity of our employees, disrupt our supply chains, delay our clinical studies, reduce our access to capital or limit our business development activities, will depend on future developments, which are highly uncertain and cannot be predicted

with confidence. To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section, such as those relating to the timing and results of our clinical studies and our financing needs.

Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our Rejuva gene therapy candidate, and any of our potential future gene therapy candidates, and adversely affect our ability to conduct our business or obtain regulatory approvals for our Rejuva gene therapy candidate.

Our Rejuva gene therapy candidate involves introducing genetic material into a patient's pancreas via endoscopic administration. Gene therapy remains a novel technology, with only a limited number of gene therapy approved to date. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of metabolic diseases targeted by our current or future gene therapy candidates, prescribing treatments that involve the use of our current or future gene therapy candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development, commercialization or demand of our current and future gene therapy candidates we develop. Potential serious adverse events in our clinical studies, or other clinical studies involving gene therapy or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our current and future gene therapy candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Risks Relating to Our Dependence on Third Parties

We substantially rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct certain aspects of our preclinical studies, and clinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain marketing authorization of or commercialize our product candidates and our business could be substantially harmed.

We substantially rely, and expect to continue to rely, on third parties, including independent clinical investigators and third-party CROs, to conduct certain aspects of our preclinical studies and to monitor and manage data for our ongoing preclinical programs. We rely on these parties for execution of our preclinical and clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We, our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of study sponsors, principal investigators and study sites. If we or any of these third parties or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical studies may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical studies before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations. In addition, our clinical studies must be conducted with product produced under cGMP or similar foreign regulations. Our failure to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process. Moreover, our business may be adversely affected if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations.

In addition, the FDA or comparable foreign regulatory authority may conclude that our financial relationships with principal investigators, some of whom we engage as consultants, have created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical study site and the utility of the clinical study itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Further, there is no guarantee that any such CROs, investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. These risks are heightened as a result of the efforts of government agencies and the CROs themselves to limit the spread of COVID-19, including quarantines and shelter-in-place orders. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other product development activities, which could affect their performance on our behalf. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical studies may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely.

Our CROs have the right to terminate their respective agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical studies warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If we decide to establish new collaborations in the future, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We may face significant competition in seeking appropriate collaborators and the related negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors.

Those factors may include the design or results of clinical studies, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

In addition, there have been a significant number of recent business combinations among large companies in our industry that have resulted in a reduced number of potential future collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may enter into collaborations in the future with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek third-party collaborators in the future for the development and commercialization of one or more of our product candidates. Our likely collaborators for any future collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates could pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical study results, changes in the collaborators' strategic focus, including as a result of a sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical studies, provide insufficient funding for a clinical study program, stop a clinical study or abandon a product candidate, repeat or conduct new clinical studies or require a new formulation of a product candidate for clinical testing;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;

- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;

- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all; and

- if a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA or foreign regulations, provide accurate information to the FDA or comparable foreign regulatory agencies, comply with federal, state and foreign health care fraud and abuse and compliance laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, submission of false claims, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting/rebating, marketing and promotion, consulting, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

Risks Related to Manufacturing

We contract with third parties for the manufacture of sub-assembly components for Revita and for the materials for our Rejuva gene therapy platform for preclinical studies and our ongoing clinical studies, and expect to continue to do so for additional clinical studies and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of sub-assembly components for Revita and for the materials for our Rejuva gene therapy platform for preclinical and clinical studies under the guidance of members of our organization. We do not have long-term supply agreements. We manage the final assembly and testing of Revita at our headquarters located in Lexington, Massachusetts, except for the sterilization of the Revita DMR catheter, which is outsourced to a third party. Furthermore, the materials for our product candidates are sourced, in some cases, from a single-source supplier. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical studies. For example, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our products and product candidates will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or study drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical study interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP or similar foreign regulations for manufacturing both active drug substances and finished drug products. For example, we are dependent on our contract manufacturing partners for the production of sub-assembly components of Revita, such as the Revita DMR catheter, Revita console and lineset. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA others, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

If we or our suppliers fail to comply with the FDA's good manufacturing practice regulations, this could impair our ability to market our products in a cost-effective and timely manner.

We and our third-party suppliers and manufacturers are required to comply with the FDA's cGMPs, which in the case of medical devices is known as the Quality System Regulation, or QSR. The QSR covers the methods and documentation of the design, testing, production, control, quality assurance, labeling, packaging, sterilization, storage and shipping of our device product candidates. The FDA audits compliance with the QSR and similar cGMPs for biologics through periodic announced and unannounced inspections of manufacturing and other facilities. The FDA may conduct inspections or audits at any time. If we or our suppliers or manufacturers have significant non-compliance issues or if any corrective action plan that we or our suppliers propose in response to observed deficiencies is not sufficient, the FDA could take enforcement action, including any of the following sanctions:

- untitled letters, warning letters, fines, injunctions, consent decrees and civil penalties;
- customer notifications or repair, replacement, refunds, recall, detention or seizure of our products;
- operating restrictions or partial suspension or total shutdown of production;
- refusing or delaying approval of a PMA, BLA or supplements thereto for new products or modified products;
- withdrawing approvals that have already been granted;
- refusal to grant export approval for our products; or
- criminal prosecution.

Any of these sanctions could have a material adverse effect on our reputation, business, results of operations and financial condition.

Outside the United States, our products and operations are also often required to comply with standards set by industrial standards bodies, such as the International Organization for Standardization, or ISO. Foreign bodies may evaluate our products or the testing that our products undergo against these standards. The specific standards, types of evaluation and scope of review differ among foreign bodies. We intend to comply with the standards enforced by such foreign bodies as needed to commercialize our products. If we fail to adequately comply with any of these standards, a foreign body may take adverse actions similar to those within the power of the FDA. Any such action may harm our reputation and business, and could have an adverse effect on our business, results of operations and financial condition.

We depend on third-party sole-source suppliers for certain sub-assembly components of Revita, and any interruption in our relationship with such third-party sole-source suppliers may materially adversely affect our business.

We rely upon third-party suppliers for the manufacture of sub-assembly components of Revita. We do not have long-term supply agreements with any of our suppliers, some of which are single- or sole-source suppliers of the relevant sub-assembly component. For example, we order sub-assembly components on a purchase-order basis from several key suppliers. We have not yet identified and qualified second-source replacements for many of our critical single-source suppliers. Thus, in the event that our relationship with any of our single- or sole-source suppliers terminates in the future, we may have difficulty maintaining sufficient supplies of key sub-assembly components of our product candidate. We may also have difficulty obtaining similar sub-assembly components from other suppliers that are acceptable to the FDA or other regulatory agencies, and the failure of our suppliers to comply with strictly enforced regulatory requirements could expose us to regulatory action including warning letters, product recalls, termination of distribution, product seizures or civil penalties. Where practicable, we are currently seeking, or intend to seek, second-source manufacturers for our single-source components.

Changes in methods of our Rejuva gene therapy candidate manufacturing or formulation may result in additional costs or delay.

As gene therapy candidates proceed through preclinical studies to late-stage clinical studies towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and product characteristics. Such alterations can also occur due to changes in manufacturers. Such changes carry the risk that they will not achieve our intended objectives. Any such changes could cause our Rejuva gene therapy candidates to perform differently and affect the results of planned clinical studies or other future clinical studies conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical studies, require the conduct of bridging clinical studies or the repetition of one or more clinical studies beyond those we currently anticipate, increase clinical study costs, delay approval of our Rejuva gene therapy candidates and jeopardize our ability to commence sales and generate revenue. In addition, we may be required to make significant changes to our upstream and downstream processes across our pipeline, which could delay the development of any future gene therapy candidates.

Any contamination or interruption in our Rejuva gene therapy candidate's manufacturing process, shortages of raw materials or failure of our suppliers of plasmids and viruses to deliver necessary components could result in delays in our Rejuva gene therapy candidate's preclinical and clinical development or marketing schedules.

Given the nature of gene therapy manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce our Rejuva gene therapy candidate or future gene therapy candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Additionally, although our Rejuva gene therapy candidate will be tested for contamination prior to release, if a contaminated

product was administered to a patient in any future clinical studies, it could result in harm to the patient. Some of the raw materials required in the manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our Rejuva gene therapy candidate could adversely impact or disrupt the commercial manufacturing or the production of preclinical and clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

If our facilities are damaged or become inoperable, we will be unable to continue to research, develop and manufacture our product candidates and, as a result, there will be an adverse impact on our business until we are able to secure a new facility.

We do not have redundant facilities. We currently perform substantially all of our research and development, manufacturing and back office activity and maintain most of our raw material and finished goods inventory in a single location in Lexington, Massachusetts. Our facility and equipment would be costly to replace and could require substantial lead time to repair or replace. The facility may be harmed or rendered inoperable by natural or man-made disasters, including, but not limited to, tornadoes, flooding, fire and power outages, which may render it difficult or impossible for us to perform our research, development, manufacturing and commercialization activities for some period of time. The inability to perform those activities, combined with our limited inventory of reserve raw materials and finished product candidates, may result in the inability to manufacture our product candidates during such periods and the delay of our ongoing or future clinical studies, including our ongoing Revitalize-1 pivotal clinical study of Revita. Although we possess insurance for damage to our property and the disruption of our business, this insurance may not be sufficient to cover all of our potential losses and this insurance may not continue to be available to us on acceptable terms, or at all.

Risks Related to Legal and Regulatory Compliance Matters

We face the risk of product liability claims that could be expensive, divert management's attention and harm our reputation and business. We may not be able to maintain adequate product liability insurance.

Our product candidates may contain undetected defects. Any such defects may prevent or impair our customers' ability to use our product candidates, if approved, and may damage our customers' businesses and could harm our reputation. If that occurs, we may incur significant costs, the attention of our key personnel could be diverted or other significant customer relations problems may arise. We may also be subject to warranty and liability claims for damages related to defects in our product candidates. A material liability claim or other occurrence that harms our reputation or decreases market acceptance of our product candidates could harm our business and operating results.

Our business exposes us to the risk of product liability claims that are inherent in the testing, manufacturing and marketing of medical devices or biopharmaceutical products. This risk exists even if a device is cleared, approved or certified for commercial sale by the FDA, foreign regulatory authorities or notified bodies and manufactured in facilities licensed and regulated by the FDA or an applicable foreign regulatory authority. Our products are designed to affect, and any future products will be designed to affect, important bodily functions and processes and may contain undetected defects. Any side effects, manufacturing defects, misuse or abuse associated with our products or our products in development could result in patient injury or death. The medical device and biopharmaceutical industries have historically been subject to extensive litigation over product liability claims, and we cannot offer any assurance that we will not face product liability suits. We may be subject to product liability claims if Revita or other products or product candidates cause, or merely appear to have caused, patient injury or death. In addition, an injury that is caused by the activities of our suppliers, such as those who provide us with sub-assembly components necessary to manufacture Revita, may be the basis for a claim against us. Product liability claims may be brought against us by consumers, healthcare providers or others selling or otherwise coming into contact with our products, among others. If we cannot successfully defend

ourselves against product liability claims, we will incur substantial liabilities and reputational harm. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- costs of litigation;
- distraction of management's attention from our primary business;
- the inability to commercialize our product candidates;
- decreased demand for our products or, if cleared, approved or certified, products in development;
- damage to our business reputation;
- product recalls or withdrawals from the market;
- withdrawal of clinical study participants;
- substantial monetary awards to patients or other claimants; or
- loss of revenue.

While we may attempt to manage our product liability exposure by proactively recalling or withdrawing from the market any defective products, any recall or market withdrawal of our products may delay the supply of those products to our customers and may impact our reputation. We can provide no assurance that we will be successful in initiating appropriate market recall or market withdrawal efforts that may be required in the future or that these efforts will have the intended effect of preventing product malfunctions and the accompanying product liability that may result. Such recalls and withdrawals may also be used by our competitors to harm our reputation for safety or be perceived by patients as a safety risk when considering the use of our products, either of which could have an adverse impact on our business.

In addition, although we have product liability and clinical study liability insurance that we believe is appropriate, this insurance is subject to deductibles and coverage limitations. Our current product liability insurance may not continue to be available to us on acceptable terms, if at all, and, if available, coverage may not be adequate to protect us against any future product liability claims. If we are unable to obtain insurance at an acceptable cost or on acceptable terms or otherwise protect against potential product liability claims, we could be exposed to significant liabilities. A product liability claim, recall or other claim with respect to uninsured liabilities or for amounts in excess of insured liabilities could have an adverse impact on our business.

We are subject to applicable fraud and abuse, transparency, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

There are numerous U.S. federal and state, as well as foreign, laws pertaining to healthcare fraud and abuse, including anti-kickback, false claims and physician transparency laws. Our business practices and relationships with physicians, hospitals and other healthcare providers are subject to scrutiny under these laws. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibit any person or entity from, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. In addition, a person or entity does not need to have actual knowledge of the statute or specific

intent to violate it in order to have committed a violation. The U.S. government has interpreted this law broadly to apply to the marketing and sales activities of manufacturers. Violations of the federal Anti-Kickback Statute may result in significant civil monetary penalties, plus up to three times the remuneration involved. Civil penalties for such conduct can further be assessed under the federal False Claims Act. Violations can also result in criminal penalties, including significant criminal fines and imprisonment of up to 10 years. Similarly, violations can result in exclusion from participation in government healthcare programs, including Medicare and Medicaid. Moreover, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act;

- the federal civil and criminal false claims laws and civil monetary penalties laws, including the federal civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other federal healthcare programs that are false or fraudulent. These laws can apply to manufacturers who provide information on coverage, coding, and reimbursement of their products to persons who bill third-party payors. Private individuals can bring FCA "qui tam" actions, on behalf of the government and such individuals, commonly known as "whistleblowers," may share in amounts paid by the entity to the government in fines or settlement. When an entity is determined to have violated the federal civil FCA, the government may impose significant civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal Civil Monetary Penalties Law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;

- the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- the federal transparency requirements under the Physician Payments Sunshine Act, created under the Affordable Care Act, which requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to report to CMS information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician's immediate family members. Beginning in 2022, applicable manufacturers will also be required to report such information regarding payments and other transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives;

- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, that may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by any non-governmental third-party payors, including private insurers; and

- state and foreign laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation and other remuneration provided to physicians and other health care providers or marketing expenditures; and state and local laws that require the registration of medical device sales representatives.

These laws and regulations, among other things, constrain our business, marketing and other promotional and research activities by limiting the kinds of financial arrangements we may have with hospitals, physicians, and other healthcare providers and potential purchases of our products, when approved. We have entered into consulting agreements with physicians, including some who have ownership interests in us, which could be viewed as influencing the purchase of or use of our products in procedures they perform. Compensation under some of these arrangements includes the provision of stock or stock options. Due to the breadth of these laws, the narrowness of statutory exceptions and regulatory safe harbors available, and the range of interpretations to which they are subject, it is possible that some of our current or future practices might be challenged under one or more of these laws.

To enforce compliance with the healthcare regulatory laws, certain enforcement bodies have recently increased their scrutiny of interactions between medical device manufacturers and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. Additionally, as a result of these investigations, manufacturers may have to agree to additional compliance and reporting requirements as part of a consent decree or corporate integrity agreement. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business, financial condition and results of operations. Even an unsuccessful challenge or investigation into our practices could cause adverse publicity, and be costly to respond to.

Any action brought against us for violations of these laws or regulations, even if successfully defended, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. We may be subject to private qui tam actions brought by individual whistleblowers on behalf of the federal or state governments, with potential liability under the federal False Claims Act including mandatory treble damages and significant per-claim penalties.

If our operations are found to be in violation of any of the federal, state and foreign laws described above or any other current or future fraud and abuse or other healthcare laws and regulations that apply to us, we may be subject to significant penalties, including significant criminal, civil, and administrative penalties, damages, fines, exclusion from participation in government programs, such as Medicare and Medicaid, imprisonment, contractual damages, reputation harm and disgorgement and we could be required to curtail, restructure or cease our operations. Any of the foregoing consequences will negatively affect our business, financial condition and results of operations.

Healthcare reform initiatives and other administrative and legislative proposals in the United States may adversely affect our business, financial condition, results of operations and cash flows.

There have been and continue to be proposals by the federal government, state governments, regulators, and third-party payors to control or manage the increased costs of healthcare and, more generally, to reform the United States healthcare system. Outside of the United States, foreign governments and regulatory authorities may implement new requirements that could impact our business and market acceptance. Certain of these

proposals could limit the prices we are able to charge for our products or limit coverage of, or lower reimbursement for, procedures associated with the use of our products , once approved, and could limit the acceptance and availability of our products. The cost containment measures that payors and providers are instituting and the effect of any healthcare reform initiative implemented in the future could impact our revenue from the sale of our products. The Affordable Care Act, or ACA, made a number of substantial changes in the way healthcare is financed by both governmental and private insurers. Among other ways in which it may affect our business, the ACA:

- imposed a new federal excise tax on the sale of certain medical devices, which was suspended, effective January 1, 2016, and permanently repealed in December 2019;
- established a new Patient-Centered Outcomes Research Institute to oversee and identify priorities in comparative clinical effectiveness research in an effort to coordinate and develop such research;
- implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models; and
- expanded the eligibility criteria for Medicaid programs.

Certain provisions of the ACA have been subject to judicial and Congressional challenges. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law, including the Tax Cuts and Jobs Act, enacted on December 22, 2017, or TCJA), which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a United States District Court Judge in the Northern District of Texas (Texas District Court Judge) ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the United States Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. In June 2021, the United States Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, upholding the ACA. Additionally, earlier in 2021, President Biden issued an executive order to initiate a special enrollment period to allow people to obtain health insurance coverage through the ACA marketplace, and instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, among others. We cannot predict how the Supreme Court ruling, other litigation, or the healthcare reform measures of the Biden administration will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, includes reductions to Medicare payments to providers of, on average, 2% per fiscal year, which went into effect on April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2030, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through the end of 2021, unless additional congressional action is taken.

Additionally, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, enacted on April 16, 2015, repealed the formula by which Medicare made annual payment adjustments to physicians and replaced the former formula with fixed annual updates and a new system of incentive payments that are based on various performance measures and physicians' participation in alternative

payment models such as accountable care organizations. It is unclear what effect new quality and payment programs, such as MACRA, may have on our business, financial condition, results of operations, or cash flows. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our products, once approved, and accordingly, our financial operations. We cannot assure you that the ACA, as currently enacted or as amended in the future, will not harm our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

We expect that other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement and downward pressure on the price that we receive for our products, once approved. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost-containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products, once marketing clearance is obtained.

We may not be able to successfully commercialize our product candidates due to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could make it difficult for us to sell our product candidates profitably.

Patients who receive treatment for their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those treatments. Patients are unlikely to use our product candidates, once approved, unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our product candidates. Therefore, coverage and adequate reimbursement are critical to a new product's acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products or procedures using these products. In the United States, there is no uniform policy among third-party payors for coverage and reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting reimbursement policies, but also have their own methods and approval processes apart from Medicare coverage and reimbursement determinations. Therefore, one third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product or procedures that use the product.

Coverage and reimbursement by a governmental and other third-party payors may depend upon a number of factors, including the third-party payor's determination that use of a product or service and its use for a particular patient is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product or procedure from a government or other third-party payor is a time-consuming and costly process, with uncertain results, that could require us to provide

supporting scientific, clinical and cost effectiveness data for the use of our product candidates to the payor. We may not be able to provide data sufficient to satisfy governmental and third-party payors that procedures using our products should be covered and reimbursed. There may be significant delays in obtaining such coverage and reimbursement for newly approved product candidates or the related procedures, and coverage may not be available, or may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities.

Reimbursement may not be available for procedures using any product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement may not be adequate. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for procedures using any approved product candidates that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates and our overall financial condition.

Outside of the United States, many countries require approval of the sale price of a product before it can be marketed, and the pricing review period only begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some of these countries, we may be required to conduct a clinical study that compares the cost-effectiveness of our product candidate to other available therapies. In some foreign markets, pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if such product candidates obtain marketing approval.

Changes in and actual or perceived failures to comply with U.S. and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and financial performance.

We and our partners may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that govern data privacy and security). The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and may increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations, including state security breach notification laws, federal and state health information privacy laws (including HIPAA), and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or applicable state laws.

We are subject to rapidly evolving data protection laws, rules and regulations in foreign jurisdictions. For example, the European Union General Data Protection Regulation, or GDPR, governs certain collection and other processing activities involving personal data about individuals in the European Economic Area. Among other things, the GDPR imposes requirements regarding the security of personal data, the rights of data subjects to access and delete personal data, requires having lawful bases on which personal data can be processed and transferred outside of the European Economic Area, requires changes to informed consent practices, and requires more detailed notices for clinical study participants and investigators. In addition, the GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our annual global revenue). The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Further, from January 1, 2021, companies are subject to the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR

mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire on June 27, 2025 unless the European Commission re-assesses and renews/extends that decision, and remains under review by the Commission during this period. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the UK will be regulated in the long term. These changes will lead to additional costs and increase our overall risk exposure.

Further, in July 2020, the Court of Justice of the European Union, CJEU, limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield Framework for purposes of international transfers and imposing further restrictions on use of the standard contractual clauses, or SCCs. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Compliance with U.S. and foreign privacy and security laws, rules and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. If we fail to comply with any such laws, rules or regulations, we may face government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation or adverse publicity that could adversely affect our business, financial condition and results of operations.

Risks Related to Our Intellectual Property

We rely on a variety of intellectual property rights, and if we are unable to obtain, maintain or protect our intellectual property, our business, financial situation, results of operations, and prospects will be harmed. If we are unable to obtain and maintain patent protection for our current product candidate, any future product candidates we may develop and our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our current product candidate, any future product candidates we may develop and our technology may be adversely affected.

Our commercial success will depend, in part, on our ability to obtain and maintain intellectual property protection for our product candidates and related technologies, including Revita, both in the United States and elsewhere, successfully defend our intellectual property rights against third-party challenges and successfully enforce our intellectual property rights to prevent third-party infringement. As with other medical device companies, we rely primarily upon a combination of patents, trademarks and trade secret protection, as well as nondisclosure, confidentiality and other contractual agreements, to protect the intellectual property related to our brands, products and other proprietary technologies.

We cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents will include, claims with a scope sufficient to protect our product

candidates or otherwise provide any competitive advantage. Our patents and any patent issuing from any of our patent applications would not prevent third-party competitors from creating, making and marketing alternative systems, devices and/or methods capable of performing similar procedures that fall outside the scope of our patent claims. There can be no assurance that any such alternative systems, devices and methods will not be equally effective as ours or that we will be able to obtain or maintain patent protection at all. Moreover, other parties have developed technologies that may be related to or competitive with our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patents or patent applications. Such third-party patent positions may limit or even eliminate our ability to obtain or maintain patent protection for certain inventions. Additionally or alternatively, such third-party patent rights may represent alternative or pre-existing technologies not protected by our own intellectual property that could be used to compete with us.

Our success depends, in part, on our ability to obtain, maintain, expand, enforce, and defend the scope of our patent portfolio or other intellectual property rights, including the amount and timing of any payments we may be required to make in connection with the filing, defense and enforcement of any patents or other intellectual property rights. The process of obtaining patent protection is expensive and time-consuming, and we may not be able to file or prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations or product candidates and may choose not to pursue patent protection in certain jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope and, in any event, any patent protection we obtain may be limited. For example, under the laws of many jurisdictions, patent protection is not available or is limited for surgical methods and certain other medical procedures. As a result, some of our product candidates may not be protected by patents in one or more jurisdictions, or, possibly, in any jurisdiction. We generally apply for patents in those countries where we intend to make, have made, use or sell product candidates and where we assess the risk of infringement to justify the cost of seeking patent protection. However, we do not and will not seek protection in all countries where we intend to sell product candidates and we may not accurately predict all the countries where patent protection would ultimately be desirable. If we fail to timely file a patent application in any such country or major market, we may be precluded from doing so at a later date. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories in which we have patent protection that may not be sufficient to terminate infringing activities. Several of our pending patent applications are in the early stages, and the deadline for deciding whether and in which jurisdictions to pursue protection has not yet expired for those applications. Prior to the applicable deadlines, we will need to decide whether and where to pursue protection, and we will not have the opportunity to obtain protection in jurisdictions where we elect not to seek protection. For other of our pending applications, the applicable timelines for deciding where to seek protection have passed, and we have made decisions, on an application-by-application basis, to pursue protection for each of those applications in a limited number of jurisdictions.

Furthermore, we cannot guarantee that any patents will be issued from any pending or future patent applications, or that any current or future patents, will provide us with any meaningful protection or competitive advantage. Even if issued, patents may be challenged, including with respect to ownership, narrowed, invalidated, held unenforceable or circumvented, any of which could limit our ability to prevent competitors and other third parties from developing and marketing similar products or limit the duration of patent protection we may have for our product candidates and technologies. Other companies may also design around technologies we have patented or developed. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our product candidates or practicing our own patented technology, including Revita. The risks described herein with respect to patents and patent applications we own similarly apply to any patents or patent applications that we may license in the future. These and other factors may prevent us from realizing any competitive advantage from patents.

The strength of patent rights generally, and particularly the patent positions of medical device companies, can be highly uncertain and involve complex legal, scientific and factual questions for which important legal principles remain unresolved. The standards that the United States Patent and Trademark Office, or the USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly. Changes in either the patent laws, implementing regulations or the interpretation of patent laws may diminish the value of our rights. The legal systems of certain countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions.

Because patent applications in the United States, Europe and many other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in our pending patent applications, or that we were the first to file for protection of the inventions set forth in our applications. We can give no assurance that all of the potentially relevant prior art relating to our patents or patent applications has been found; overlooked prior art could be used by a third-party to challenge the validity, enforceability and scope of our patents, or prevent a patent from issuing from a pending patent application. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the validity, enforceability and scope of our patents in the United States, Europe and in other countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against our competitors.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity or enforceability. Third parties may challenge any existing patent or future patent we own or license through adversarial proceedings in the issuing offices or in court proceedings, including as a response to any assertion of our patents against them. In any of these proceedings, a court or agency with jurisdiction may find our patents invalid and/or unenforceable, or even if valid and enforceable, insufficient to provide protection against competing products and services to achieve our business objectives. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or reexamination by the USPTO if a third-party asserts a substantial question of patentability against any claim of a U.S. patent we own or license. The adoption of the Leahy-Smith America Invents Act, or the Leahy-Smith Act, in September 2011 established additional opportunities for third parties to invalidate U.S. patent claims, including *inter partes* review and post-grant review proceedings. Outside of the United States, patents we own or license may become subject to patent opposition or similar proceedings, which may result in loss of scope of some claims or the entire patent. Competitors may claim that they invented the inventions claimed in our patents or pending applications prior to the inventors of our intellectual property, or may have filed for protection for certain inventions before we did. We may need to participate in interference or derivation proceedings, which may result in the loss of some or all of the patent protection at issue. Furthermore, an adverse decision in an interference or derivation proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. Any of these proceedings may be very complex and expensive, and may divert our management's attention from our core business. If any of our patents, should they issue, are challenged, invalidated, circumvented by third parties or otherwise limited or expire prior to the commercialization of our product candidates, and if we do not own or have exclusive rights to other enforceable patents protecting our product candidates or other technologies, competitors and other third parties could market products and use processes that are substantially similar or identical to, or superior to, ours and our business would suffer.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates or the related technologies in all countries and jurisdictions throughout the world would be prohibitively expensive, and we will only pursue

patent protection in selected jurisdictions outside the United States. The requirements for patentability differ in various countries. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and the laws of some foreign countries do not provide patent protection for certain types of inventions that are patentable in the United States. As a result, certain aspects of our technology may not be protectable by patents or may be difficult to protect in certain jurisdictions outside the United States, including in Europe, and our intellectual property rights outside the United States could be less extensive than those in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For some of the patent families owned by us, the relevant statutory deadlines have not yet expired, and we will need to decide whether and where to pursue protection outside the United States before expiration of the applicable deadlines. For other of the patent families owned by us, the relevant statutory deadlines have expired, and thus, we will only have the opportunity to pursue protection in the limited jurisdictions previously selected.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, if approved, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to medical technology. For example, an April 2021 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. This could make it difficult for us to stop the infringement of our patents or the misappropriation or other violation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. We may choose not to initiate lawsuits because the expected benefit is not sufficient. Accordingly, our efforts to enforce our intellectual property rights outside the United States may be inadequate to obtain a significant commercial advantage from the intellectual property.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

The medical device industry has been characterized by extensive litigation regarding patents, trademarks, trade secrets, and other intellectual property rights, and companies in the industry have used intellectual property litigation to gain a competitive advantage. Litigation or other legal proceedings related to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming. Competitors may infringe our patents, should they issue, or other intellectual property, or we may be required to defend against claims of infringement, misappropriation or other violation of third party intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that our patents are invalid or unenforceable or that we infringe their intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, which could adversely affect our competitive business position, business prospects and financial condition.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating, or otherwise violating, or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation or continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Our commercial success depends significantly on our ability to operate without infringing, misappropriating or otherwise violating the intellectual property rights of third parties.

The medical device industry is subject to rapid technological change and substantial litigation regarding patent and other intellectual property rights. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use, market and sell our product candidates and technology.

Numerous third-party patents exist in the fields relating to our product candidates, and it is difficult for industry participants, including us, to identify all third-party patent rights relevant to our product candidates and technologies. We are aware of third-party patents, and patent applications that if issued, may be construed to cover our product candidates or technologies, including Revita. There may be issued U.S. or European patents of which we are not aware, held by our competitors or third parties that, if found to be valid and enforceable, could

be alleged to be infringed by some of our product candidates or technologies, including Revita. We are also aware of pending patent applications, and there may be others of which we are not aware, that if they result in issued patents, could be alleged to be infringed by some of our product candidates or technologies, including Revita. Moreover, because some patent applications are maintained as confidential for a certain period of time, we cannot be certain that third parties have not filed patent applications that cover our product candidates and technologies.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates or technology because database searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our product candidates or technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not-infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates and technologies. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. Our determination of the expiration date of any patent in the United States, the European Union or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates.

Patents could be issued, now or in the future, to third parties that we may ultimately be found to infringe. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing product candidates using our technology. Our failure to obtain or maintain a license to any technology that we require may materially harm our business, financial condition, results of operations and prospects. Furthermore, we would be exposed to a threat of litigation. In addition, we may be required or choose to enter into a license agreement to avoid or settle litigation.

Intellectual property rights of third parties could adversely affect our ability to commercialize our product candidates, and we might be required to litigate or obtain licenses from third parties in order to develop or market our product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms.

From time to time, we may be party to, or threatened with, litigation or other proceedings with third parties, including non-practicing entities, who allege that our product candidates, components of our product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. The types of situations in which we may become a party to such litigation or proceedings include:

- we may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our product candidates, technologies, or processes do not infringe those third parties' patents;
- we may participate at substantial cost in International Trade Commission proceedings to abate importation of products or product candidates that would compete unfairly with our product candidates;
- if our competitors file patent applications that claim technology also claimed by us, we may be required to participate in interference, derivation or opposition proceedings to determine the priority

of invention, which could jeopardize our patent rights and potentially provide a third-party with a dominant patent position;

- if third parties initiate litigation claiming that our processes or product candidates infringe their patent or misappropriate or otherwise violate other intellectual property rights, we will need to defend against such proceedings;
- if third parties initiate litigation or other proceedings seeking to invalidate patents owned by us or to obtain a declaratory judgment that their product or technology does not infringe our patents, we will need to defend against such proceedings;
- we may be subject to ownership disputes relating to intellectual property, including disputes arising from conflicting obligations of employees or consultants or others who are involved in developing our product candidates; and
- if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or product candidates infringe their patent or misappropriate or otherwise violate other intellectual property rights and/ or that we breached our obligations under the license agreement, and we would need to defend against such proceedings.

These lawsuits and proceedings, regardless of merit, are time-consuming and expensive to initiate, maintain, defend or settle, and could divert the time and attention of managerial and technical personnel, which could materially adversely affect our business. Any such claim could also force use to do one or more of the following:

- incur substantial monetary liability for infringement, appropriation or other violations of intellectual property rights, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party's rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the third party's attorneys' fees;
- pay substantial damages to our customers or end users to discontinue use or replace infringing technology with non-infringing technology;
- stop manufacturing, selling, using, exporting or licensing the product candidate or technology incorporating the allegedly infringing technology or stop incorporating the allegedly infringing technology into such product candidate or technology;
- obtain from the owner of the infringed intellectual property right a license, which may require us to pay substantial upfront fees or royalties to sell or use the relevant technology and which may not be available on commercially reasonable terms, or at all;
- redesign our product candidates and technology so they do not infringe, misappropriate or violate the third party's intellectual property rights, which may not be possible or may require substantial monetary expenditures and time;
- enter into cross-licenses with our competitors, which could weaken our overall intellectual property position;
- lose the opportunity to license our technology to others or to collect royalty payments based upon successful protection and assertion of our intellectual property against others;

- find alternative suppliers for non-infringing product candidates and technologies, which could be costly and create significant delay; or

- relinquish rights associated with one or more of our patent claims, if our claims are held invalid or unenforceable.

The medical device industry is characterized by extensive litigation regarding patents and other intellectual property rights. As we continue to develop and, if approved, commercialize our current product candidates and future product candidates, competitors may claim that our products, product candidates or technology infringe, misappropriate or otherwise violate their intellectual property rights as part of business strategies designed to impede our successful commercialization. As we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or technologies may be subject to claims of infringement, misappropriation or other violation of the intellectual property rights of third parties. There may be third-party patents or patent applications with claims related to a product candidate or our technology, such as to Revita. Because patent applications can take many years to issue, third parties may have currently pending patent applications that may later result in issued patents that our product candidates may infringe, or which such third parties claim are infringed by our technologies. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, to prevail, we would need to demonstrate that our product candidates, products, technologies or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings. Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause shipment delays of product candidates, or prohibit us from manufacturing, marketing or otherwise commercializing our product candidates and technology. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operation, financial condition or cash flows.

In addition, we may indemnify our customers and distributors against claims relating to the infringement of intellectual property rights of third parties related to our product candidates or technologies. Third parties may assert infringement claims against our customers or distributors. These claims may require us to initiate or defend protracted and costly litigation on behalf of our customers or distributors, regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of our customers, suppliers or distributors, or may be required to obtain licenses for the products they use. If we cannot obtain all necessary licenses on commercially reasonable terms, our customers may be forced to stop using our product candidates.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. The occurrence of any of these events may have a material adverse effect on our business, results of operation, financial condition, prospects or cash flows.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our existing and future product candidates and technologies.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our patents. On September 16, 2011, the Leahy-Smith America Invents Act or the Leahy-Smith Act was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, and may also affect patent litigation. The USPTO developed new regulations and procedures to govern administration of the Leahy-Smith Act, including switching the United States patent system from a "first-to-invent" system to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. For example, a third party that files a patent application before us at the USPTO could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. Additional provisions of the Leahy-Smith Act allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent through various proceedings, including post-grant review and inter partes review proceedings, administered by the USPTO. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our patents, should they issue, all of which could have a material adverse effect on our business, results of operation, financial condition or cash flows.

In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our patents and applications. Furthermore, the U.S. Supreme Court and the U.S. Court of Appeals for the Federal Circuit have made, and will likely continue to make, changes in how the patent laws of the United States are interpreted. Similarly, foreign courts have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by United States and foreign legislative bodies. Those changes may materially affect our patents or patent applications and our ability to obtain additional patent protection in the future.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees and various government fees are due to be paid to governmental patent agencies over the lifetime of a patent. Future maintenance fees will also need to be paid on other patents that may be issued to us. We have systems in place to remind us to pay these fees, and we employ outside firms to remind us or our licensor to pay annuity fees due to patent agencies on our patents and pending patent applications. In certain cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in

abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business, results of operation, financial condition, prospects or cash flows.

Patent terms may not be sufficient to effectively protect our product candidates and business for an adequate period of time.

Patents have a limited lifespan. In the United States, the natural expiration of a utility patent is generally 20 years after its first effective non-provisional filing date. Although various extensions may be available, the term of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, proprietary technologies and their uses are obtained, once the patent has expired, we may be open to competition, which may harm our business prospects. In addition, although upon issuance in the United States a patent's term can be extended based on certain delays caused by the USPTO, this extension can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. Given the amount of time required for the development, testing and regulatory review of new products, patents protecting such products might expire before or shortly after such products are commercialized. If we do not have sufficient patent terms to protect our products, proprietary technologies and their uses, our business would be seriously harmed. As our patents expire, the scope of our patent protection will be reduced, which may reduce or eliminate any competitive advantage afforded by our patent portfolio. As a result, our reduced patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We rely on trademarks and tradenames to distinguish our product and technology from the products of our competitors. Our registered or unregistered trademarks or trade names may be challenged, opposed, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we rely on to build name recognition among potential partners and customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks, such as those that incorporate variations of our registered or unregistered trademarks or trade names. An adverse decision in a trademark or trade name suit may subject us to damages, and may result in the need to redesign or rename the infringing brand, which could be costly and time-consuming. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Moreover, as our products mature, our reliance on our trademarks to differentiate us from our competitors will increase, and as a result, if we are unable to prevent third parties from adopting, registering or using trademarks and trade dress that infringe, dilute or otherwise violate our trademark rights, or engaging in conduct that constitutes unfair competition, defamation or other violation of our rights, our business could be materially adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks and trade names, may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets and other proprietary information, our business and competitive position may be harmed.

In addition to patent protection, we also rely on confidential proprietary information, including trade secrets and know-how, to develop and maintain our competitive position. However, trade secrets and other

proprietary information can be difficult to protect and some courts are less willing or unwilling to protect trade secrets and proprietary information. We seek to protect our confidential proprietary information, in part, by entering into confidentiality agreements with our employees, consultants, vendors, collaborators and others, upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential. Our agreements with employees, business consultants, and our personnel policies, also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, the assignment of intellectual property rights may not be self-executing, and individuals with whom we have these agreements may not comply with their terms or may have preexisting or competing obligations to third parties of which we are not aware. Thus, despite such agreements, such inventions may become assigned to third parties. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third-party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all, and the failure to obtain rights in such intellectual property by assignment or license could have a material adverse effect on our business.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. We and our contractors and partners operate in certain countries that are at heightened risk of theft of technology, data and intellectual property through direct or indirect intrusion by private parties or international actors, including those affiliated with or controlled by state actors. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations. Further, it is possible that others will independently develop the same or similar technology or otherwise obtain access to our unpatented technology, and in such cases we could not assert any trade secret rights against such parties. Costly and time consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. In addition, others may independently discover or develop our trade secrets and proprietary information, and the existence of our own trade secrets affords no protection against such independent discovery.

We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

We may also employ individuals, such as employees, consultants or advisors, who were previously or are concurrently employed at or providing consulting services for research institutions and/or other medical

device companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may be subject to claims that these employees, consultants or advisors, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former or concurrent employers, or that patents and applications we have filed to protect inventions of these employees, consultants or advisors, even those related to one or more of our product candidates or technologies, are rightfully owned by their former or concurrent employer. Additionally, we may be subject to claims from third parties challenging our ownership interest in intellectual property we regard as our own, based on claims that our employees, consultants or advisors have breached an obligation to assign inventions to another employer, to a former employer, or to another person or entity. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable personnel or intellectual property rights. An inability to incorporate such technologies or features would have a material adverse effect on our business and may prevent us from successfully commercializing our product candidates. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would have an adverse effect on our business, results of operations and financial condition.

We may enter into licenses to intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing a product candidate, if approved, that relied on such licensed intellectual property.

We may in the future be party to license agreements under which we are granted rights to material intellectual property that is important to our business. We would expect any such license agreements to impose various obligations on us, including but not limited to, diligence obligations and the payment of milestones and/or royalties. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our business could suffer, for example, if any material licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents or other forms intellectual property do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation.

Additionally, we may collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are

acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

We may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the drug candidates that we license from third parties. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than if we conduct them ourselves. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our drugs that are subject of such licensed rights could be adversely affected.

Licensing of intellectual property involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our right to transfer or assign the license;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the priority of invention of patented technology; and
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

In addition, license agreements are often complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or broaden what we believe to be the scope of a licensor's rights to our intellectual property and technology, or increase what we believe to be our financial or other obligations under a relevant agreement, any of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. If disputes over intellectual property impair our ability to maintain any future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. Furthermore, certain of our future agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, we may in the future enter into license agreements that are not assignable or transferable, or that require the licensor's express consent in order for an assignment or transfer to take place.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to

entry against our competitors or potential competitors, or permit us to maintain any competitive advantage. Moreover, if a third party has intellectual property rights that cover a product candidate or the practice of our technology, such as Revita, we may not be able to fully exercise or extract value from our intellectual property rights. We cannot ensure that:

- any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates or otherwise provide any competitive advantage;
- any of our pending patent applications will issue as patents at all;
- we were the first to make inventions covered by any of our existing patent applications;
- we were the first to file patent applications for our inventions;
- we have not omitted that should be listed as inventors or included individuals that should not be listed as inventors in our patents and patent applications, which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- others will not develop similar or alternative technologies that do not infringe our intellectual property, incorporate technology from the public domain, or will otherwise be able to design around our patents, should they issue;
- others will not use preexisting technology to effectively compete against us;
- any of our patents, if issued, will ultimately be found to be valid and enforceable;
- there are no prior public disclosures that could invalidate our patents, or parts of our patents;
- that there are no unpublished, third-party patent applications or applications maintained in secrecy that may later issue with claims covering our product candidate or technology;
- third parties will not compete with us in jurisdictions where we do not pursue and obtain patent protection;
- the laws of foreign countries will protect our proprietary rights to the same extent as the laws of the United States;
- the inventors of our patents or patent applications will not become involved with competitors to develop products or processes that design around our patents;
- any patents issued to us will provide a basis for an exclusive market for our commercially-viable products, if approved, or provide us with any competitive advantages, or will not be challenged by third parties; or
- our commercial activities or products will not infringe upon the patents or proprietary rights of others.

Should any of these events occur, they could significantly harm our business and results of operations.

Risks Related to Employee Matters and Managing Our Growth

If we are unable to establish sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval.

We currently do not have and have never had a marketing or sales team. In order to commercialize any product candidates, if approved, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our product candidates. We may not be successful in accomplishing these required tasks.

Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time-consuming, and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval or certification to market, if we do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or certification or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. In particular, we are highly dependent on the management and business expertise of Harith Rajagopalan, M.D., Ph.D., our Chief Executive Officer, Jay D. Caplan, our Chief Product Officer, and Lisa A. Davidson, our Chief Financial Officer, each of whom is employed by us at will. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our results of operations. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the medical device and pharmaceutical industries is intense and as a result, we may be unable to continue to attract and retain qualified personnel necessary for the future success of our business. We could in the future have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other medical device and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of March 31, 2022, we have 83 full-time employees, including 67 employees engaged in research and development. In order to successfully implement our development and commercialization plans and strategies, and as we transition into operating as a public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA and other comparable foreign regulatory agencies' or notified bodies' review process of our current product candidates and any other product candidate we develop, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and, if approved, commercialize Revita and any other product candidate will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third party service providers is compromised for any reason, our clinical studies may be extended, delayed or terminated, and we may not be able to obtain marketing approval of any current or future product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize Revita and any other current or future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Risks Related to This Offering and Ownership of Our Common Stock

There has been no prior public market for our common stock. We do not know whether an active, liquid and orderly trading market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Prior to this offering, no public market for shares of our common stock existed and an active trading market for our common stock may never develop or be sustained following this offering. We determined the initial public offering price for our common stock through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of our common stock after this offering. The market value of our common stock may decrease from the initial public offering price. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you

consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies, technologies or other assets by using our shares of common stock as consideration.

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock following this offering is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. The trading prices for common stock of other pharmaceutical and biotechnology companies have also been highly volatile as a result of the COVID-19 pandemic.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this prospectus, these factors include:

- the timing and results of preclinical and clinical studies of our product candidates or those of our competitors;
- the success of competitive products or announcements by potential competitors of their product development efforts;
- regulatory actions with respect to our product candidates or our competitors' products;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- market conditions in the pharmaceutical and biotechnology sector;
- changes in the structure of healthcare payment systems;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- expiration of market stand-off or lock-up agreements;

- the ongoing and future impact of the COVID-19 pandemic, or any future public health crises, including epidemics and pandemics, and actions taken to slow their spread; and

- general economic, industry and market conditions.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

Our management team has broad discretion to use the net proceeds from this offering and its investment of these proceeds may not yield a favorable return. They may invest the net proceeds from this offering in ways with which investors disagree.

We plan to use the net proceeds from this offering to fund the ongoing Revitalize-1 pivotal clinical study of Revita, the Revitalize-2 pivotal study, and the Revitalize-3 pilot study; the continued preclinical development of our Rejuva gene therapy platform; for medical education and market development, and other commercial readiness activities; and for working capital and other general corporate purposes. See "Use of Proceeds." However, within the scope of our plan, and in light of the various risks to our business, including those discussed in this "Risk Factors" section and elsewhere in this prospectus, our management will have broad discretion over the use of net proceeds from this offering, and could spend the net proceeds in ways our stockholders may not agree with or that do not yield a favorable return, if at all. If we do not invest or apply the net proceeds from this offering in ways that improve our results of operations, we may fail to achieve expected financial results, which could cause our stock price to decline.

If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. We do not currently have and may never obtain research coverage by securities or industry analysts. If no or few securities or industry analysts commence coverage of us, the stock price would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our results of operations fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Prior to this offering, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 69% of our voting stock and, upon the closing of this offering, that same group will beneficially own approximately % of our outstanding voting stock. Therefore, even after this offering these stockholders will be able to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

If you purchase shares of our common stock in our initial public offering, you will experience substantial and immediate dilution.

The initial public offering price of our common stock is substantially higher than the net tangible book value (deficit) per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after this offering. Based on the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $ per share, representing the difference between our pro forma as adjusted net tangible book value per share after this offering and the assumed initial public offering price. This dilution is due in large part to the fact that our earlier investors paid substantially less than the initial public offering price when they purchased their shares of our capital stock. In addition, as of December 31, 2021, we had outstanding stock options to purchase an aggregate of 17,738,374 shares of common stock at a weighted-average price of $1.51 per share. To that extent, you will experience additional dilution when those holding stock options exercise their right to purchase common stock under our equity incentive plans or when we otherwise issue additional shares of common stock. See "Dilution."

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Our common stock price could decline as a result of sales of a large number of shares of common stock after this offering or the perception that these sales could occur. These sales, or the possibility that these sales may occur, might also make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate.

Upon the completion of this offering, shares of common stock will be outstanding (shares if the underwriters exercise their option to purchase additional shares from us in full), based on the number of shares outstanding as of December 31, 2021.

All shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless held by our "affiliates" as defined in Rule 144 under the Securities Act. The resale of the remaining shares, or approximately % of our outstanding shares of common stock following this offering, is currently prohibited or otherwise restricted as a result of securities law provisions, market standoff agreements entered into by certain of our stockholders with us or lock-up agreements entered into by our stockholders with the underwriters in connection with this offering. However, subject to applicable securities law restrictions, these shares will be able to be sold in the public market beginning 181 days after the date of this prospectus. Shares issued upon the exercise of stock options and warrants outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, market stand-off agreements and/or lock-up agreements, as well as Rules 144 and 701 under the Securities Act. For more information, see "Shares Eligible for Future Sale."

Upon the completion of this offering, the holders of approximately shares, or approximately % of our outstanding shares following this offering, of our common stock will have rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or our other stockholders. We also intend to register the offer and sale of all shares of common stock that we may issue under our equity compensation plans. Once we register the offer and sale of shares for the holders of registration rights and shares that may be issued under our equity incentive plans, these shares will be able to be sold in the public market upon issuance, subject to the lock-up agreements described under "Underwriting."

In addition, in the future, we may issue additional shares of common stock, or other equity or debt securities convertible into common stock, in connection with a financing, acquisition, employee arrangement or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause the price of our common stock to decline.

We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock.

We have never declared or paid any cash dividends on our equity securities. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of our common stock, which is not certain.

Provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our certificate of incorporation and bylaws, as we expect they will be in effect upon closing of the offering, will contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan (also known as a "poison pill");
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting;
- authorize our board of directors to amend the bylaws;
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and
- require a super-majority vote of stockholders to amend some provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our certificate of incorporation, bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws will provide for an exclusive forum in the Court of Chancery of the State of Delaware for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the Court of Chancery of the State of Delaware (or, in the event that the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws will also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause or causes of action against any defendant arising under the Securities Act. Such provision is intended to benefit and may be enforced by us, our officers and directors, employees and agents, including the underwriters and any other professional or entity who has prepared or certified any part of this prospectus. Nothing in our amended and restated certificate of incorporation or amended and restated bylaws preclude stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

We believe these provisions may benefit us by providing increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims or make such lawsuits more costly for stockholders, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive-forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

General Risks

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors, consultants, collaborators or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants, collaborators and third-party service providers, are vulnerable to damage from computer viruses, cybersecurity threats, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failure. If such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of or access to health-related or other personal information, it could result in a material disruption of our drug discovery and development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Notifications and follow-up actions related to a security breach could impact our reputation, cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical study data from completed or future clinical studies could result in delays in our regulatory approval or certification efforts and significantly increase our costs to recover or reproduce the lost data. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and/or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

Our operations are vulnerable to interruption by fire, severe weather conditions, power loss, telecommunications failure, terrorist activity, future pandemics and other events beyond our control, which could harm our business.

Our facilities are located in regions which experience severe weather from time to time. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major tornado, flood, fire, earthquake, power loss, terrorist activity, future pandemics or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we intend to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on financial statements;
- reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements; and
- exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We intend to take advantage of the extended transition period for adopting new or revised accounting standards under the JOBS Act as an emerging growth company. As a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates.

We are a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are considered a "smaller reporting company." We are therefore entitled to rely on certain reduced disclosure requirements for as long as we remain a smaller reporting company, such as an exemption from providing selected financial data and executive compensation information. If we qualify as a smaller reporting company because we meet the revenue limits under the definition of a smaller reporting company, we will be a "low-revenue smaller reporting company." Low-revenue smaller reporting companies are not required to obtain an external audit on the effectiveness of their internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404. These exemptions and reduced disclosures may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our

common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

The requirements of being a public company may strain our resources, result in more litigation and divert management's attention.

As a public company, we will be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, the listing requirements of Nasdaq and other applicable securities rules and regulations. Complying with these rules and regulations has increased and will increase our legal and financial compliance costs, make some activities more difficult, time consuming or costly and increase demand on our systems and resources. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and results of operations. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are required to disclose changes made in our internal control and procedures on a quarterly basis. In order to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight may be required. As a result, management's attention may be diverted from other business concerns, which could adversely affect our business and results of operations. We may also need to hire additional employees or engage outside consultants to comply with these requirements, which will increase our costs and expenses.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

These new rules and regulations may make it more expensive for us to obtain director and officer liability insurance and, in the future, we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

By disclosing information in this prospectus and in future filings required of a public company, our business and financial condition will become more visible, which we believe may result in threatened or actual litigation, including by competitors and other third parties. If those claims are successful, our business could be seriously harmed. Even if the claims do not result in litigation or are resolved in our favor, the time and resources needed to resolve them could divert our management's resources and seriously harm our business.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are a smaller reporting company, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

Changes in our effective tax rate or tax liability may have an adverse effect on our results of operations.

We are subject to income taxes in the United States. Our effective tax rate could be adversely affected due to several factors, including:

- changes in the relative amounts of income before taxes in the various jurisdictions in which we operate that have differing statutory tax rates;
- changes in the United States tax laws and regulations or the interpretation of them, including the Tax Act, as modified by the CARES Act;
- changes to our assessment about our ability to realize our deferred tax assets that are based on estimates of our future results, the prudence and feasibility of possible tax planning strategies, and the economic and political environments in which we do business;
- the outcome of current and future tax audits, examinations, or administrative appeals; and
- limitations or adverse findings regarding our ability to do business in some jurisdictions.

New income or other tax laws or regulations could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws and regulations could be interpreted, modified, or applied adversely to us. For example, the Tax Act enacted many significant changes to the U.S. tax Laws. Future guidance from the IRS and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Act, and proposed legislation currently under consideration by Congress in connection with the 2022 U.S. federal budget reconciliation may result in significant changes to tax law enacted under the Tax Act. Changes in corporate tax rates, the realization of net operating losses, and other deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets and could increase our future U.S. tax expense.

If our product candidates are approved, we expect to generate a portion of our future revenue internationally and are subject to various risks relating to international operations, which could adversely affect our operating results.

We believe that a portion of our future revenue will come from international sources as we plan to seek regulatory approvals of our product candidates in international markets and, if approved, to establish overseas operations. Engaging in international business involves a number of difficulties and risks, including:

- required compliance with existing and changing foreign healthcare and other regulatory requirements and laws, such as those relating to patient privacy or handling of bio-hazardous waste;
- required compliance with anti-bribery laws, such as the U.S. Foreign Corrupt Practices Act and U.K. Bribery Act, data privacy requirements, labor laws and anti-competition regulations;
- export or import restrictions;
- various reimbursement and insurance regimes;
- laws and business practices favoring local companies;
- longer payment cycles and difficulties in enforcing agreements and collecting receivables through certain foreign legal systems;
- political and economic instability;
- potentially adverse tax consequences, tariffs, customs charges, bureaucratic requirements and other trade barriers;
- foreign exchange controls;
- difficulties and costs of staffing and managing foreign operations;
- difficulties protecting or procuring intellectual property rights; and
- existence of additional third-party intellectual property rights of potential relevance.

If the value of the U.S. dollar increases relative to foreign currencies in the future, in the absence of a corresponding change in local currency prices, our future revenue could be adversely affected as we convert future revenue from local currencies to U.S. dollars.

If we dedicate resources to our international operations and are unable to manage these risks effectively, our business, operating results and prospects will suffer.

New tax legislation may impact our results of operations and financial condition.

The U.S. government may enact significant changes to the taxation of business entities including, among others, an increase in the corporate income tax rate and the imposition of minimum taxes or surtaxes on certain types of income. For example, In connection with the 2022 U.S. federal budget reconciliation, Congressional committees have proposed changes in tax law that could result in additional federal income taxes being imposed on us. If such changes are enacted or implemented, we are currently unable to predict the ultimate impact on our business.

Taxing authorities may successfully assert that we should have collected or in the future should collect sales and use, value added or similar taxes, and any such assessments could adversely affect our business, financial condition, and results of operations.

Sales and use, value added and similar tax laws and rates vary greatly by jurisdiction. Certain jurisdictions in which we do not collect such taxes may assert that such taxes are applicable or that our presence in such jurisdictions is sufficient to require us to collect taxes, which could result in tax assessments, penalties and interest, and we may be required to collect such taxes in the future. Such tax assessments, penalties and interest or future requirements may adversely affect our financial condition and results of operations. Further, in June 2018, the Supreme Court held in South Dakota v. Wayfair, Inc. that states could impose sales tax collection obligations on out-of-state sellers even if those sellers lack any physical presence within the states imposing the sales taxes. Under the Wayfair decision, a person requires only a "substantial nexus" with the taxing state before the state may subject the person to sales tax collection obligations therein. An increasing number of states (both before and after the publication of the Wayfair decision) have considered or adopted laws that attempt to impose sales tax collection obligations on out-of-state sellers. The Supreme Court's Wayfair decision has removed a significant impediment to the enactment and enforcement of these laws, and it is possible that states may seek to tax out-of-state sellers on sales that occurred in prior tax years, which could create additional administrative burdens for us, put us at a competitive disadvantage if such states do not impose similar obligations on our competitors, and decrease our future sales, which could adversely affect our business, financial condition, and results of operations.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that can involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, future revenue, timing and likelihood of success, plans and objectives of management for future operations, future results of anticipated products and prospects, plans and objectives of management are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” ,” “potential,” “predict,” “project,” “should,” “target,” “will,” or “would” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the timing, progress and results of preclinical and clinical studies for our current and future product candidates, including statements regarding the timing of initiation and completion of studies and related preparatory work, the period during which the results of the studies will become available and our research and development programs;
- the timing, scope or likelihood of regulatory submissions, filings, clearances and approvals, including final regulatory approval or clearance of our product candidates;
- our ability to develop and advance product candidates into, and successfully complete, clinical studies;
- our expectations regarding the size of the patient populations for our product candidates, if approved or cleared for commercial use;
- the implementation of our business model and our strategic plans for our business, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy, as well as our product development strategy;
- the pricing and reimbursement of our product candidates, if approved or cleared;
- the scalability and commercial viability of our manufacturing methods and processes, including our plans to maintain our in-house manufacturing facility, even after commercialization of any of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our competitive position;
- the scope of protection we and/or any future licensors are able to establish and maintain for intellectual property rights covering our product candidates;

- developments and projections relating to our competitors and our industry;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements;
- the impact of laws and regulations;
- our expectations regarding the time during which we will be an emerging growth company and smaller reporting company under the JOBS Act; and
- the impact of the COVID-19 pandemic and potential future public health crises, including epidemics and pandemics.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

We estimate that the net proceeds to us from in this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares from us is exercised in full, we estimate that our net proceeds will be approximately $ million.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, by $ million, assuming the assumed initial public offering price stays the same.

We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $ million to fund the ongoing Revitalize-1 pivotal clinical study;
- approximately $ million to fund the planned Revitalize-2 pivotal study;
- approximately $ million to fund the planned Revitalize-3 pilot study;
- approximately $ million to fund the continued preclinical development of our Rejuva gene therapy platform;
- approximately $ million to fund medical education and market development, and other commercial readiness activities; and
- the remainder for working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We may also use a portion of the net proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Predicting the cost necessary to develop product candidates can be difficult and we anticipate that we will need additional funds to complete the development of any product candidates we identify. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from preclinical studies and any ongoing clinical studies or studies we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements

through . We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities. We cannot predict whether the proceeds invested will yield a favorable return.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to fund the development, commercialization and growth of our business, and therefore we do not anticipate declaring or paying any cash dividends on any class of our common stock in the foreseeable future. Any future determination as to the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to compliance with contractual restrictions and covenants in the agreements governing our current and future indebtedness. Any such determination will also depend upon our business prospects, results of operations, financial condition, cash requirements and availability and other factors that our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Accordingly, you may need to sell your shares of our common stock to realize a return on your investment, and you may not be able to sell your shares at or above the price you paid for them. See “Risk Factors—Risks Related to This Offering and Ownership of Our Common Stock—We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock.”

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2021, as follows:

- on an actual basis;
- on a pro forma basis to give effect to (i) the repayment in full of all outstanding borrowings under our Loan and Security Agreement in January 2022 for a total amount of $16.1 million, (ii) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 77,994,156 shares of our common stock, as if such conversion had occurred on December 31, 2021, (iii) the receipt of approximately $20.1 million in cash proceeds from the sale of the 2022 Notes in January 2022, (iv) the automatic settlement of the 2022 Notes, including accrued interest, into shares of our common stock in connection with the closing of this offering, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus, (v) an aggregate charge to accumulated deficit of $ relating to the loss resulting from the settlement of the 2022 Notes, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus, and (vi) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information below is illustrative only, and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our consolidated financial statements and the related notes included elsewhere in this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections and other financial information contained in this prospectus.

	As of December 31, 2021		
(in thousands, except for share and per share amounts)	Actual	Pro Forma (unaudited)	Pro Forma As Adjusted(1) (unaudited)
Cash and cash equivalents	$ 95,473	$	$
Convertible preferred stock warrant liability	$ 544	$	$
Convertible preferred stock, par value $0.00001 per share: 78,112,639 shares authorized, 77,994,156 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	287,330		
Stockholders' equity (deficit):			
Preferred stock, $0.00001 par value per share: no shares authorized, issued and outstanding, actual; shares authorized, pro forma and pro forma as adjusted; no shares issued and outstanding, pro forma and pro forma as adjusted	—		

(in thousands, except for share and per share amounts)	As of December 31, 2021		
	Actual	Pro Forma (unaudited)	Pro Forma As Adjusted(1) (unaudited)
Common stock, $0.00001 par value per share: 107,000,000 shares authorized, 4,049,782 shares issued and outstanding, actual; shares authorized, pro forma and pro forma as adjusted; shares issued and outstanding, pro forma; shares issued and outstanding, pro forma as adjusted	—		
Additional paid-in capital	13,747		
Accumulated deficit	(223,072)		
Total stockholders' equity (deficit)	(209,325)		
Total capitalization	$ 78,549		

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization by approximately $ million.

The information in the table above excludes:

- 17,738,374 shares of our common stock issuable upon exercise of outstanding stock options granted under the 2011 Plan as of December 31, 2021, at a weighted average exercise price of $1.51 per share;
- 4,131,844 shares of our common stock available for future issuance under the 2011 Plan as of December 31, 2021, which such shares will cease to be available for issuance at the time our 2022 Plan becomes effective;
- shares of common stock that will become available for future issuance under the 2022 Plan, which will become effective in connection with the completion of this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2022 Plan;
- shares of common stock that will become available for future issuance under the ESPP, which will become effective in connection with the completion of this offering, and shares of our common stock that become available pursuant to provisions in the ESPP that automatically increase the share reserve under the ESPP; and
- 465,315 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2021, at a weighted average exercise price of $1.53 per share.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

Our historical net tangible book value (deficit) as of December 31, 2021 was $(211.5) million, or $(52.23) per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and preferred stock, which is not included within stockholders' equity (deficit). Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by the 4,049,782 shares of our common stock outstanding as of December 31, 2021.

Our pro forma net tangible book value (deficit) as of December 31, 2021 was $ million, or $ per share of our common stock. Pro forma net tangible book value per share is determined by subtracting our total liabilities from the total book value of our tangible assets and dividing the difference by the number of shares of common stock deemed to be outstanding, after giving effect to (i) the repayment in full of all outstanding borrowings under our Loan and Security Agreement in January 2022 for a total amount of $16.1 million, (ii) the receipt of approximately $20.1 million in cash proceeds from the sale of the 2022 Notes in January 2022, (iii) the automatic settlement of the 2022 Notes, including accrued interest, into shares of our common stock in connection with the closing of this offering, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus, (iv) an aggregate charge to accumulated deficit of $ to the loss resulting from the settlement of the 2022 Notes, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus, and (v) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 77,994,156 shares of common stock as if such conversion had occurred on December 31, 2021.

After giving further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share (which is the midpoint of the price range set forth on the cover page of this prospectus) and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2021, would have been $ million, or $ per share of common stock. This amount represents an immediate increase in pro forma as adjusted net tangible book value of $ per share to our existing stockholders and an immediate dilution in pro forma as adjusted net tangible book value of $ per share to new investors purchasing shares of common stock in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per share after this offering from the amount of cash that a new investor paid for a share of common stock.

The following table illustrates this dilution:

Assumed initial public offering price per share of common stock		$
Historical net tangible book value (deficit) per share as of December 31, 2021	$(52.23)	
Increase per share attributable to the issuance of the 2022 Notes, the conversion of outstanding convertible preferred stock and settlement of the 2022 Notes		
Pro forma net tangible book value per share as of December 31, 2021 before this offering		
Increase in pro forma as adjusted net tangible book value per share attributable to investors in this offering		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to new common stock investors in this offering		$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by approximately $, and dilution in pro forma as adjusted net tangible book value per share to new investors by approximately $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase an additional shares of our common stock in this offering in full, the pro forma as adjusted net tangible book value of our common stock would increase to $ per share, representing an immediate increase to existing stockholders of $ per share and an immediate dilution of $ per share to new investors participating in this offering.

The following table summarizes, as of December 31, 2021, after giving effect to this offering, the number of shares of our common stock purchased from us, the total consideration paid, or to be paid, to us and the average price per share paid, or to be paid, by existing stockholders and by the new investors. The calculation below is based on an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders (1)					
New investors					
Total		**100%**		**100%**	

(1) The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases that existing stockholders may make in this offering.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the total consideration paid by new investors and the total consideration paid by all stockholders by $ million, assuming the number of shares offered by us remains the same and after deducting estimated underwriting discounts and commissions but before estimated offering expenses.

If the underwriters exercise their option to purchase additional shares of our common stock in full, the total consideration paid by new investors and the average price per share paid by new investors would be approximately $ million and $ per share, respectively, in each case assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus.

Except as otherwise indicated, the discussion and the tables above assume no exercise of the underwriters' option to purchase additional shares of our common stock and excludes:

- 17,738,374 shares of our common stock issuable upon exercise of outstanding stock options granted under the 2011 Plan as of December 31, 2021, at a weighted average exercise price of $1.51 per share;
- 4,131,844 shares of our common stock available for future issuance under the 2011 Plan as of December 31, 2021, which such shares will cease to be available for issuance at the time our 2022 Plan becomes effective;

- shares of common stock that will become available for future issuance under the 2022 Plan, which will become effective in connection with the completion of this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2022 Plan;

- shares of common stock that will become available for future issuance under the ESPP, which will become effective in connection with the completion of this offering, and shares of our common stock that become available pursuant to provisions in the ESPP that automatically increase the share reserve under the ESPP; and

- 465,315 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2021, at a weighted average exercise price of $1.53 per share.

To the extent any of these outstanding options or warrants are exercised, there will be further dilution to new investors. To the extent all of such outstanding options had been exercised as of December 31, 2021, the pro forma as adjusted net tangible book value per share after this offering would be $, and total dilution per share to new investors would be $.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the sections titled "Summary Consolidated Financial Data" and our consolidated financial statements and related notes and other information included elsewhere in this filing. In addition to historical data, this discussion contains forward-looking statements about our business, results of operations, cash flows, financial condition and prospects based on current expectations that involve risks, uncertainties and assumptions. Our actual results could differ materially from such forward-looking statements. Factors that could cause or contribute to those differences include, but are not limited to, those identified below and those discussed in the sections titled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" included elsewhere in this filing. Additionally, our historical results are not necessarily indicative of the results that may be expected for any period in the future. We use words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "seek," "should," "will," "would," and similar expressions to identify forward-looking statements.

Business Overview

We are an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes, or T2D. Despite advances in treatment over the last 50 years, metabolic diseases in general, and T2D in particular, continue to be a principal and rapidly growing driver of morbidity and mortality in the 21st century. The International Diabetes Federation estimates that nearly 600 million people are expected to be living with T2D globally by 2035. In the United States alone, the Centers for Disease Control and Prevention estimates that nearly 27 million people have been diagnosed with T2D. A study published by Fang et al. in the New England Journal of Medicine in 2021 reported that glycemic control is worsening in this population and approximately half of these individuals are not achieving targeted disease control despite the availability of over 60 approved drugs for the condition. Our goal is to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. The Revita DMR System, or Revita, our lead product candidate, is designed to remodel the duodenal lining via hydrothermal ablation in order to edit abnormal intestinal nutrient sensing and signaling mechanisms that we believe are a root cause of metabolic diseases. Led by our ongoing Revitalize-1 pivotal study, we have initiated a broad clinical program, Revitalize T2D, designed to evaluate Revita in multiple concurrent clinical studies across a range of patient populations from prediabetes to T2D patients on long-acting insulin. In addition, we are developing Rejuva, a novel pancreatic gene therapy platform, to enable long-term remission of T2D by potentially restoring insulin production in patients with advanced disease. We believe our product candidates, if approved, have the potential to revolutionize the treatment of T2D, align the interest of key stakeholders in the disease, and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

Since our formation in 2010, we have devoted substantially all of our efforts and financial resources to organizing and staffing our company, business planning, raising capital, acquiring or discovering product candidates and securing related intellectual property rights and conducting discovery, research and development activities for our product candidates. We do not have any products approved for sale in the United States and have not generated any revenue from any sources, including product sales. We obtained a Conformite` Europe□enne, or CE, mark for Revita in Europe in 2016. However, we do not currently market this product in any territory. To date, we have financed our operations primarily through sales of our convertible preferred stock and term loans drawn under our loan and security agreements, or Term Loans, with Silicon Valley Bank, or SVB. In January 2022, we sold and issued approximately $20.1 million aggregate principal amount of convertible promissory notes, or the 2022 Notes, in a private placement transaction.

We have incurred significant operating losses since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates. For the years ended December 31,

2021 and 2020, we incurred net losses of $38.7 million and $30.5 million, respectively. As of December 31, 2021, we had an accumulated deficit of $223.1 million. We expect to continue to incur significant losses for the foreseeable future and we expect these losses to increase substantially if and as we:

- advance the development of Revita and Rejuva through preclinical and clinical development, and, if approved by the FDA or other comparable foreign regulatory authorities, commercialization;
- incur manufacturing costs for our product candidates;
- increase our manufacturing capacity;
- seek regulatory approvals for any of our product candidates that successfully complete clinical studies;
- increase our research and development activities to identify and develop new product candidates;
- hire additional personnel;
- expand our operational, financial and management systems;
- invest in measures to protect and expand our intellectual property;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval and intend to commercialize;
- expand our manufacturing and develop our commercialization efforts; and
- operate as a public company.

We do not anticipate generating revenue from product sales unless and until we successfully complete clinical development and obtain marketing approvals for one or more of our product candidates, if ever. We are currently establishing our commercial infrastructure to support the anticipated marketing and distribution of our product candidates. Subject to receiving marketing approval, we may to enter into arrangements with third parties for the sale, marketing and distribution of our product candidates. Accordingly, if we obtain marketing approval for any of our product candidates, we will incur significant additional commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations with other companies and strategic alliances. We may not be able to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we would have to significantly delay, reduce or eliminate the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Impact of the COVID-19 Pandemic

In December 2019, SARS-CoV-2, a novel strain of coronavirus that causes COVID-19, was first identified globally. On March 11, 2020, the World Health Organization declared COVID-19 a global pandemic. Since then, COVID-19 has caused significant disruptions and adverse economic impacts across multiple countries, including the United States. To date, we have maintained uninterrupted business operations. We have

implemented adjustments to our operations designed to keep employees safe and comply with federal, state and local guidelines, including those regarding social distancing, and have transitioned administrative functions to predominantly remote work. As a result of the COVID-19 pandemic, we reduced headcount and were forced to delay our commercial launch efforts in the United Kingdom due to reduced patient access to hospitals and clinics.

Beginning in March 2020 and continuing through the end of 2021, the ongoing COVID-19 pandemic has reduced patient access to clinical laboratories, causing a decrease in enrollment and a temporary suspension of certain trials. The extent to which COVID-19 may further impact our business, results of operations, financial condition and cash flows will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

Components of our Consolidated Results of Operations

Revenue

To date, we have not generated any revenue, and do not expect to generate any revenue from the sale of products for the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval or collaboration or license agreements with third parties, we may generate revenue in the future from product sales or payments from collaboration or license agreements that we may enter into with third parties, or any combination thereof. We cannot predict if, when or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates in the United States.

Operating Expenses

Research and Development Expenses

Research and development expenses primarily consist of personnel-related expenses, including salaries, bonuses, fringe benefits and other compensation-related costs, including stock-based compensation expense, for employees engaged in research and development functions. Research and development expenses also include costs of conducting our ongoing clinical studies, such as expenses associated with our clinical research organization, or CRO, who provides project management and other services related to our Revitalize-1 study, outside service fees paid to third party consultants and contractors related to our product candidate engineering, quality assurance and regulatory approval, contract manufacturing of our product candidate used in clinical studies as well as research expenses related to our Rejuva gene therapy platform.

We expense research and development costs as incurred. Non-refundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and other long-term assets, which are expensed as the related goods are delivered or the services are performed, or when it is no longer expected that the goods will be delivered or the services rendered.

A significant portion of our research and development costs have been, and will continue to be, external costs. We track these external costs, such as fees paid to CROs, preclinical study vendors and other third parties in connection with our product engineering, sub-assembly component manufacturing and manufacturing process development, clinical studies, preclinical studies and other research activities on a program-by-program basis. We also use a portion of our personnel and infrastructure resources for our research and development efforts, which are shared across multiple programs under development, and as such, are not tracked on a program-by-program basis. The following table reflects our research and development expense, including direct

program-specific expense summarized by program, indirect expenses, and personnel-related expenses recognized during each period presented (in thousands):

(in thousands)	Year Ended December 31, 2021	2020
Direct program-specific expenses:		
Revita	$ 11,036	$ 10,169
Rejuva	1,489	1,149
Total direct program-specific expenses	12,525	11,318
Indirect expenses	2,436	2,194
Personnel-related expenses (including stock-based compensation)	11,474	8,921
Total research and development expenses	$26,435	$22,433

We expect our research and development expenses will increase significantly in the future as we:

- hire and retain additional personnel, including research, clinical, development, manufacturing, quality control, quality assurance, regulatory and scientific personnel;
- continue to conduct our ongoing Revitalize-1 pivotal study, including additional clinical studies under our Revitalize T2D program;
- continue to advance the research and development of our discovery and preclinical programs, such as Rejuva;
- seek regulatory approval for any product candidates that successfully complete clinical studies; and
- develop, establish and validate our commercial-scale current good manufacturing practices and manufacturing process.

General and Administrative Expenses

General and administrative expenses primarily consist of personnel-related costs, including salaries, bonuses, fringe benefits and other compensation-related costs, including stock-based compensation expense, for our personnel and external contractors involved in our executive, finance, legal and other administrative functions as well as our commercial function, who is involved in market access related activities. General and administrative expenses also include costs incurred for outside services associated with such functions, including costs associated with obtaining and maintaining our patent portfolio and professional fees for accounting, auditing, tax, legal services and other consulting expenses.

We anticipate that our general and administrative expenses will increase significantly in the future as we:

- hire and retain additional general and administrative personnel to support the expected growth in our research and development activities and the potential commercialization of our product candidates;
- continue to expand our commercial function to support potential future product launches;
- incur additional commercialization expenses prior to any regulatory approval of our product candidates;

- pursue payor coverage and reimbursement for our current and future product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- incur increased expenses associated with operating as a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services, director and officer insurance premiums, and investor and public relations costs.

Other Expenses, Net

Interest Expense, Net

Interest expense, net primarily consists of cash and non-cash interest related to our Term Loans partially offset by interest income earned on our cash and cash equivalent balances.

Change in Fair Value of Convertible Preferred Stock Warrant Liability

The convertible preferred stock warrant liability relates to a warrant to purchase shares of our Series B convertible preferred stock. We remeasure the fair value of this convertible preferred stock warrant liability at each reporting date, with any adjustments being recorded as a component of other expenses. We will continue to recognize changes in the fair value of the warrant liability until the warrants are exercised, expire or qualify for equity classification. In connection with this offering, our convertible preferred stock warrants will convert into common stock warrants and we expect the liability will be reclassified to additional paid-in capital.

Critical Accounting Policies and Significant Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities and recorded amounts of expenses that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions. Our management has also considered the potential impact of the COVID-19 pandemic on our estimates and assumptions. The extent to which the COVID-19 pandemic may impact management's estimates in future periods is uncertain and subject to change.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this prospectus, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates. Accordingly, these are the policies we believe are the most critical to aid in fully understanding and evaluating our audited consolidated financial condition and results of operations.

Stock-Based Compensation

We measure all stock options and other stock-based awards based on their fair value on the date of the grant. Those awards typically have a graded vesting schedule and compensation expense for awards with only service conditions are recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. Compensation costs recognized for performance-based awards reflect the

number of awards that are expected to vest during the requisite service period and are adjusted to reflect those awards that ultimately vest upon final determination of the performance conditions achieved. Historical performance patterns, to the extent that they are indicative to the performance conditions to be achieved, are used in developing estimates for the probability of attaining these performance conditions.

We use the Black-Scholes option pricing model, which incorporates assumptions and estimates, to measure the fair value of its option awards on the date of grant of each stock option award.

We determined the assumptions for the Black-Scholes option-pricing model as discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

- *Fair Value of Our Common Stock*. Prior to this offering, our stock was not publicly traded, and therefore we estimated the fair value of our common stock, as discussed in "Determination of the Fair Value of Common Stock" below.

- *Expected Term*. The expected term represents the period that the stock-based awards are expected to be outstanding. As we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term, the expected term of stock options granted has been determined using the simplified method, which is the average of the midpoints between the vesting date and the contractual term for all vesting tranches.

- *Risk-Free Interest Rate*. The risk-free interest rate is based on the rate of the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award.

- *Expected Volatility*. Because we do not have a trading history of our common stock, the expected volatility was derived from the average historical stock volatilities of several public companies within our industry that we consider to be comparable to our business over a period equivalent to the expected term of the stock-based awards.

- *Dividend Rate*. The expected dividend is zero as we have not paid and do not anticipate paying any dividends in the foreseeable future.

If any of the assumptions used in the Black-Scholes model change significantly, stock-based compensation for future awards may differ materially compared with the awards granted previously.

Determination of the Fair Value of Common Stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from management, considering independent third-party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant. These independent third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. We estimated the value of our equity using market approaches. In conducting the valuations, our board of directors, with input from management, considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold convertible preferred stock and the superior rights and preferences of the convertible preferred stock relative to our common stock at the time of each grant;

- the progress of our research and development programs, including the status of preclinical studies and current status of our ongoing clinical studies;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the therapeutics and medical device industry, and trends within the therapeutics and medical device industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or a sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the therapeutics and medical device industry.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment.

When estimating the value of our equity, we applied a hybrid approach by performing a scenario-based analysis, in which we estimated the probability-weighted value across multiple scenarios. In one scenario, the equity value was determined by back-solving overall equity value to the price paid by recent financing transactions. The fair value of our equity was then allocated to various securities within our capital structure by applying an option pricing method. The option pricing method estimates the fair value of each class of security based on the potential to profit from the upside of the business, while taking into account the unique characteristics of each class of security. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the convertible preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. We also considered an IPO scenario in which the shares of convertible preferred stock are assumed to convert to common stock at the time of the IPO. The future value of the common stock under each scenario is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock.

We performed common stock valuations at various dates, which resulted in fair value of our common stock of $1.81, $3.25, $5.59 and $5.52 per share as of February 2020, April 2021, October 2021, and December 2021, respectively. The February 2020 common stock valuation was based on the equity value derived from the subsequent Series E Convertible Preferred Stock financing closed in March through July 2020. The April 2021 common stock valuation was based on the equity value derived from the subsequent Series F Convertible Preferred Stock financing closed in June and July 2021. The October 2021 and December 2021 common stock valuation was based on a probability weighted equity value considering both the value derived from the June 2021 Series F Convertible Preferred Stock financing and the estimated value at the IPO. The principal factors contributing to the increase in the valuation of our common stock from the April 2021 valuation to the October 2021 valuation were the consideration of the probability-weighting of the IPO scenario and a decrease in the discount for lack of marketability, which reflected our progress toward an IPO event.

There are significant judgments and estimates inherent in these valuations. These judgments and estimates include assumptions regarding our future operating performance, the stage of development of our product candidates, the timing and probability of a potential initial public offering or other liquidity event and the

determination of the appropriate valuation methodology at each valuation date. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation expense could be materially different.

Once a public trading market for our common stock has been established in connection with the consummation of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options, as the fair value of our common stock will be determined based on the trading price of our common stock on the Nasdaq Global Market.

The following table summarizes by grant date and type of award, the number of equity-based awards granted between January 1, 2020 and the date of this prospectus, the per share exercise price, the fair value of common stock on each grant date and the per share estimated fair value of the awards:

Grant Date	Type of Award	Number of Shares Subject to Awards Granted	Per Share Exercise Price	Fair Value of Common Stock on Grant Date	Per Share Estimated Fair Value of Awards on Grant Date
March 26, 2020	Stock option	3,173,892	$ 1.81	$ 1.81	$ 0.88
June 17, 2020	Stock option	110,000	$ 1.81	$ 1.81	$ 0.90
September 23, 2020	Stock option	330,000	$ 1.81	$ 1.81	$ 0.93
December 10, 2020	Stock option	34,990	$ 1.81	$ 1.81	$ 0.94
June 24, 2021	Stock option	2,138,793	$ 3.25	$ 3.25	$ 1.77
September 15, 2021	Stock option	120,000	$ 3.25	$ 3.25	$ 1.72
March 8, 2022	Stock option	1,032,000	$ 5.52	$ 5.52	$ 2.98

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including central laboratories and research organizations, in connection with preclinical development activities and our research programs;
- CROs and investigative sites in connection with preclinical and clinical studies; and
- Clinical Manufacturing Organizations in connection with devices and consumables used in the clinical studies.

We base our expenses related to preclinical and clinical studies on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical and clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the

expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical study milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Results of Operations

Years Ended December 31, 2021 and 2020

The following table summarizes our consolidated results of operations for the years ended December 31, 2021 and 2020:

	Year Ended December 31,		Change	
(in thousands)	**2021**	**2020**	**Amount**	**%**
Operating expenses:				
Research and development	$ 26,435	$ 22,433	$ 4,002	17.8%
General and administrative	10,493	6,528	3,965	60.7%
Total operating expenses	36,928	28,961	7,967	27.5%
Loss from operations	(36,928)	(28,961)	(7,967)	27.5%
Other expenses, net				
Interest expense, net	(1,442)	(1,503)	61	(4.1%)
Change in fair value of convertible preferred stock warrant liability	(356)	(15)	(341)	2,273.3%
Other expenses, net	(9)	(1)	(8)	800.0%
Total other expenses, net	(1,807)	(1,519)	(288)	19.0%
Net loss and comprehensive loss	$(38,735)	$(30,480)	$(8,255)	27.1%

Year Ended December 31, 2021 Compared to Year Ended December 31, 2020

Operating Expenses

Research and Development Expenses

Research and development expenses increased by $4.0 million, or 17.8%, during the year ended December 31, 2021 as compared to the year ended December 31, 2020, primarily due to increased personnel related expenses and clinical expenditures in the Revitalize-1 study. Personnel related expenses, including salaries, bonuses and certain fringe benefits, increased by $2.5 million mainly due to the new hiring in the medical and clinical department to facilitate the Revitalize-1 study as well as the rollout of the company-wide bonus program. In addition, stock-based compensation increased by $0.3 million due to the additional equity awards granted to new and existing employees. Clinical study expenses increased by $1.8 million due to the increased spending on ongoing clinical studies primarily related to the initiation of our Revitalize-1 study. Expenditures incurred in the Rejuva program also increased by $0.4 million as the program progresses. These increases were partially offset by a decrease of $1.0 million in production related expenses as we purchased most of the materials and increased production of the devices and consumables in 2020 to prepare for the initiation of the Revitalize-1 study.

General and Administrative Expenses

General and administrative expenses increased by $4.0 million, or 60.7%, during the year ended December 31, 2021 as compared to the year ended December 31, 2020, primarily due to $3.1 million of increased spending on professional fees and consulting fees, including legal, accounting, auditing, human resources, marketing and public relations services, to support our preparation to become a public company as well as market research activities. Personnel related expenses, including salaries, bonuses and certain fringe benefits, increased by $0.7 million mainly due to increased administrative personnel headcount to support the growth of the business as well as the rollout of the company-wide bonus program. Stock-based compensation also increased by $0.2 million due to the additional equity awards granted to new and existing employees.

Other Expenses, Net

Change in Fair Value of Convertible Preferred Stock Warrant Liability

Change in fair value of convertible preferred stock warrant liability increased by $0.3 million during the year ended December 31, 2021 as compared to the year ended December 31, 2020 primarily due to higher increase in the value of the underlying Series B Convertible Preferred Stock.

Liquidity and Capital Resources

We believe that we maintain a level of liquidity sufficient to allow us to meet our cash needs in the short-term. Over the long-term, we manage our cash and capital structure to maximize shareholder return, maintain its financial condition and maintain flexibility for future strategic initiatives. We continuously assess our working capital needs, debt and leverage levels, debt maturity schedule, capital expenditure requirements and future investments.

As of December 31, 2021, we had approximately $95.5 million in cash and cash equivalents. We believe that our cash and cash equivalents at December 31, 2021 will be sufficient to fund our current operating plan for at least 12 months from the issuance date of this prospectus.

Loan and Security Agreement

In February 2019, we entered into a loan and security agreement with SVB, or the 2019 Note, that provided for borrowings of up to $15.0 million in two Term Loan advances defined as “Term A Loan” and “Term B Loan”, collectively referred to as the Term Loans. On February 5, 2019, we drew down $3.0 million under Term A Loan, and on May 31, 2019, we drew down an additional $7.0 million under Term A Loan. On October 3, 2019, we drew down $5.0 million under Term B Loan.

The outstanding balances under the Term Loans bear interest at a floating annual rate that equals the greater of 1.5% above the Wall Street Journal prime rate or 6.75%. The Term Loans initially required interest-only repayments through December 31, 2020. After the interest-only period, the Term Loans require 24 equal monthly principal repayments of the outstanding balances plus accrued interest through the maturity date on December 1, 2022.

On the date that the 2019 Note is paid in full or becomes due and payable, we will make a payment, or the Final Payment, in addition to the regular monthly payments of principal plus accrued interest, equal to 6% of the original principal amount of the Term Loans extended by the lender. The Final Payment is being accreted as additional interest expense over the term of the respective Term Loans using the effective interest rate method.

In February 2019, in connection with entering into the 2019 Note, we issued to SVB and an affiliated investor warrants to purchase up to an aggregate of 257,380 shares of our common stock, at an exercise price of

$1.55 per share, or the 2019 Warrants. Of the 257,380 shares, 171,606 shares were exercisable upon the issuance of the warrants and an additional 85,774 shares became exercisable upon the drawdown of the Term B Loan. The 2019 Warrants have a contractual term of ten years from the date of issuance. We recorded the total fair value of the 2019 Warrants of $0.3 million as debt discount and additional paid-in capital. The debt discount is being amortized as additional interest expense over the term of the respective Term Loans using the effective interest rate method. As of December 31, 2021, the 2019 Warrants have not been exercised.

On December 31, 2020 and February 26, 2021, we entered into two amendments to the 2019 Note, or the Amendments, whereby the Term Loans were amended to extend the interest-only period through December 31, 2021, upon achievement of certain clinical milestone as specified in the Amendments, with principal to be repaid equally over 12 consecutive calendar months starting January 1, 2022. In connection with entering into the first Amendment, we issued to SVB and an affiliated investor, warrants to purchase up to an aggregate of 89,452 shares of the our common stock, at an exercise price of $1.81 per share, or the 2020 Warrants. The 2020 Warrants expire ten years from the date of issuance. We recorded the total fair value of the 2020 Warrants of $0.1 million as debt discount and additional paid-in capital. The debt discount is being amortized as additional interest expense over the term of the respective Term Loans using the effective interest rate method. As of December 31, 2021, the 2020 Warrants have not been exercised.

As of December 31, 2021, we had outstanding balance of the Term Loans under the Loan and Security Agreement of $15.7 million, including accreted Final Payment of $0.8 million and net of debt discount of $0.1 million. As of December 31, 2020, we had outstanding balance of the Term Loans under the Loan and Security Agreement of $15.3 million, including accreted Final Payment of $0.5 million and net of debt discount of $0.2 million.

On January 3, 2022, we repaid in full the Term Loans under the Loan and Security Agreement by making a lump-sum payment to SVB for a total amount of $16.1 million, which consisted of the outstanding principal balance of the Term Loans of $15.0 million, the Final Payment of $0.9 million, the prepayment premium of $0.1 million and accrued interest of $0.1 million.

Convertible Promissory Notes

In January 2022, we sold and issued approximately $20.1 million aggregate principal amount of convertible promissory notes in a private placement transaction, which mature on July 11, 2023, if not previously converted to common stock or preferred stock or repaid in cash. The convertible promissory notes will convert to common stock upon the completion of this offering.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we advance our product candidate. We do not have any products approved for sale in the United States and have not generated any revenue from any sources, including product sales. We obtained a CE mark for Revita in Europe in 2016. However, we do not currently market this product in any territory. In addition, upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future.

As of December 31, 2021, we had cash and cash equivalents of $95.5 million. We believe that our existing cash and cash equivalents, together with the net proceeds from this offering, will enable us to fund our operating expenses, debt repayment obligations and capital expenditure requirements into . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with product development, and because the extent to which we may enter into collaborations with third parties for the development of our product candidates

is unknown, we may incorrectly estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our funding requirements and timing and amount of our operating expenditures will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of research and development for our current and future product candidates, including our current and planned Revita clinical studies, and ongoing preclinical development for our current and future product candidates;
- the scope, prioritization and number of our research and development programs;
- the scope, costs, timing and outcome of regulatory review of our product candidates;
- the costs of securing manufacturing materials for use in preclinical and clinical studies and, for any product candidates for which we receive regulatory approval, use as commercial supply;
- our ability to seek, establish and maintain a collaboration to develop our product candidate with a collaborator, including the financial terms and any cost-sharing arrangements of any such collaboration;
- the costs and timing of future commercialization activities for any of our product candidates for which we receive regulatory approval;
- the amount and timing of revenue, if any, received from commercial sales of any product candidates for which we receive regulatory approvals;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims;
- the extent to which we may acquire or in-license other products, product candidates, technologies or intellectual property, as well as the terms of any such arrangements;
- the impacts of the COVID-19 pandemic; and
- the costs of continuing to expand our operations and operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical studies is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales in the United States. We obtained a CE mark for Revita in Europe in 2016. However, we do not currently market this product in any territory. In addition, our product candidates, if approved, may not achieve commercial success. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Our expectation with respect to our ability to fund current planned operations is based on estimates that are subject to risks and uncertainties. Our operating plan may change as a result of many factors currently unknown to management and there can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, and we may need to seek additional funds sooner than planned.

Adequate additional funds may not be available to us on acceptable terms, or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or convertible debt

securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Additional debt financing and convertible preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interest.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may have to significantly delay, reduce or eliminate some or all of our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

For additional information on risks associated with our substantial capital requirements, please see "Risk Factors—Risks Related to Financial Condition and Capital Requirements."

Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and development programs or future commercialization efforts.

Cash Flows

Years Ended December 31, 2021 and 2020

The net change in cash, cash equivalents and restricted cash for the years ended December 31, 2021 and 2020 was as follows:

	Year Ended December 31,	
(in thousands)	**2021**	**2020**
Net cash used in operating activities	$(33,462)	$(31,073)
Net cash used in investing activities	(51)	(2)
Net cash provided by financing activities	99,879	54,390
Net increase in cash and cash equivalents	$ 66,366	$ 23,315

Operating Activities

Cash used in operating activities for the year ended December 31, 2021 was primarily driven by personnel related expenses, including salaries, bonuses, and fringe benefits, as well as spending on our ongoing clinical studies. Our net loss of $38.7 million was partially offset by non-cash items totaling $3.6 million, including $0.7 million of depreciation expense, $2.1 million of stock-based compensation expense, $0.4 million of non-cash interest expense related to the debt accretion and amortization of debt discount associated with the Term Loans and $0.4 million change in fair value of convertible preferred stock warrant liability. Cash used in operating activities was also impacted by changes in working capital and other assets and liabilities of $1.7 million, primarily due to timing of vendor payments.

Cash used in operating activities for the year ended December 31, 2020 was primarily driven by personnel related expenses, including salaries, bonuses, and fringe benefits, as well as spending on our ongoing clinical studies. Our net loss of $30.5 million was partially offset by non-cash items totaling $2.9 million,

including $0.8 million of depreciation expense, $1.6 million of stock-based compensation expense and $0.5 million of non-cash interest expense related to the debt accretion and amortization of debt discount associated with the Term Loans. Cash used in operating activities was also impacted by changes in working capital and other assets and liabilities of $3.5 million, primarily related to vendor deposits associated with the initiation of clinical studies.

Investing Activities

Cash used in investing activities for the years ended December 31, 2021 and 2020 were both related to the purchase of property and equipment.

Financing Activities

Cash provided by financing activities have consisted of capital raised to fund our operations, debt borrowings from accredited financial institutions and proceeds received from exercises of stock options.

Cash provided by financing activities of $99.9 million for the year ended December 31, 2021 was primarily driven by capital raised from the issuance of Series F Convertible Preferred Stock, net of issuance costs.

Cash provided by financing activities of $54.4 million for the year ended December 31, 2020 was primarily driven by capital raised from the issuance of Series E Convertible Preferred Stock, net of issuance costs.

Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our Term Loans require payment of interest only until January 1, 2022 at a floating annual rate that equals the greater of 1.5% above the Wall Street Journal prime rate or 6.75%. We do not believe that an immediate 10% increase or decrease in the Wall Street Journal prime rate would have a material effect on our operating results. On January 3, 2022, we repaid in full the Term Loans under the Loan and Security Agreement.

Credit Risk

As of December 31, 2021, our cash and cash equivalents were maintained at a major financial institution in the United States, and our current deposits are in excess of insured limits. We believe the financial institution we maintain our cash and cash equivalents in has sufficient assets and liquidity to conduct their operations in the ordinary course of business with little or no credit risk to us.

Foreign Currency Risk

Substantially all of our business is currently conducted in U.S. dollars. We do not believe that an immediate 10% increase or decrease in the relative value of the U.S. dollar to other currencies would have a material effect on our operating results.

Inflation Risk

Inflationary factors, such as increases in our operating expenses, may adversely affect our operating results. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, a high rate of inflation in the future may significantly increase our operating expenses.

Recent Accounting Pronouncements

See Note 2 to our audited Consolidated Financial Statements for the years ended December 31, 2021 and 2020 included elsewhere in this prospectus for more information.

JOBS Act Accounting Election

We are an "emerging growth company" within the meaning of the Jumpstart Our Business Act of 2012, or JOBS Act. Section 107(b) of the JOBS Act provides that an emerging growth company can leverage the extended transition period, provided in Section 102(b) of the JOBS Act, for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. We have elected to use this extended transition period and, as a result, our financial statements may not be comparable to companies that comply with public company effective dates. We also intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002.

We would cease to be an emerging growth company on the date that is the earliest of (1) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (2) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (3) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous three years or (4) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

A Letter From Our Co-Founder

In the course of human history, metabolic diseases like type 2 diabetes have recently emerged as the principal constraint on human health, longevity and productivity. In the United States alone, nearly 27 million people are diagnosed with T2D and approximately half of these individuals are not achieving targeted disease control. By 2030, we will be spending $2 trillion a year worldwide combating this disease (and still losing). If we want a healthier society, we need to unlock a better approach to treating diabetes and other related metabolic diseases.

I have unfortunately seen firsthand how type 2 diabetes can have devastating physical and mental implications for those afflicted with the disease. I have observed the impact of diabetes not only as a cardiologist and researcher, but also as a son to a father struggling with the disease and its burdensome daily management. I have been constantly frustrated observing people living with diabetes, including my father, who continue to worsen as they battle this debilitating disease despite their best efforts using today's available treatments. Disease progression continues to worsen in our patients despite decades of investment and research and an ever-increasing number of disease management options. The current treatment paradigm is simply not working for most people living with type 2 diabetes.

Many people mistakenly assume that type 2 diabetes is simply the fault of people who make poor choices and then suffer the consequences of these choices. There is a lot of blaming and shaming of patients with type 2 diabetes in the United States, driven by a mindset that assumes behavioral weakness, human error, and lack of self-care. We believe this blame mindset is not only wrong, but dangerous. It's dangerous because we have allowed ourselves to consider these diseases as gluttonous problems of human choice rather than correctable problems of human physiology.

Our bodies are simply not designed for the abundant food environment of the modern world. We are built for an ancient world, a world in which food was scarce, not particularly tasty, and often not available when it was needed. Our ancestors, whose genes allowed them to survive through difficult times, passed those very same genes down to us – genes that now significantly increase the risk of type 2 diabetes in the modern world. This disease of excess blood sugar has arisen as an unintended, yet inevitable, consequence of this mismatch between our ancient genes and our modern dietary environment.

My co-founder, Jay Caplan, and I started Fractyl Health with the belief that a better understanding of the root causes of type 2 diabetes will create a pathway to new and better solutions that can address the significant residual unmet need in the treatment of the disease. We have assembled a mission-driven team full of innovators, united in a passion to develop therapies aiming to eradicate type 2 diabetes—the type of therapies we would want for our family members and loved ones with the disease.

Fractyl Health's purpose is to defend humanity from the metabolic diseases of modernity. Over the past several years, we have gained a deeper understanding of the changes that occur in the gut in response to modern diets. We are singularly focused on developing therapies that are designed to target the root causes of metabolic diseases and delivering our therapies as broadly as possible to as many patients as possible as rapidly as possible.

We believe this approach is better for patients, better for physicians and better for society. Turning the tide on type 2 diabetes is achievable, but it requires intestinal fortitude. It takes guts.

Co-Founder and Chief Executive Officer

BUSINESS

Overview

We are an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes, or T2D. Despite advances in treatment over the last 50 years, metabolic diseases in general, and T2D in particular, continue to be a principal and rapidly growing driver of morbidity and mortality in the 21st century. The International Diabetes Federation estimates that nearly 600 million people are expected to be living with T2D globally by 2035. In the United States alone, the Centers for Disease Control and Prevention, or the CDC, estimates that nearly 27 million people have been diagnosed with T2D. A study published in the New England Journal of Medicine in 2021 reported that glycemic control is worsening in this population and approximately half of these individuals are not achieving targeted disease control despite the availability of over 60 approved drugs for the condition. We believe we are experts in understanding the root cause of metabolic diseases in the gut. Our goal is to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. The Revita DMR System, or Revita, our lead product candidate, is designed to remodel the duodenal lining via hydrothermal ablation in order to edit abnormal intestinal nutrient sensing and signaling mechanisms that we believe are a root cause of metabolic diseases. Led by our ongoing Revitalize-1 pivotal study, we have initiated a broad clinical program, Revitalize T2D, designed to evaluate Revita in multiple concurrent clinical studies across a range of patient populations from prediabetes to T2D patients on long-acting insulin. In addition, we are developing Rejuva, a novel pancreatic gene therapy platform, to enable long-term remission of T2D by potentially restoring insulin production in patients with advanced disease. We believe our product candidates, if approved, have the potential to revolutionize the treatment of T2D, align the interest of key stakeholders in the disease, and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

T2D is a disorder of rising blood glucose that is caused by a multitude of factors, which lead to two parallel, progressive disease processes within the body: insulin resistance and insulin insufficiency. Insulin resistance is the body's inability to respond appropriately to an insulin signal to remove glucose from the bloodstream, whereas insulin insufficiency is the gradual failure of the pancreas to produce sufficient insulin to meet the body's needs. Guidelines today focus on managing the blood glucose symptoms of T2D, often measured by blood concentrations of glycosylated hemoglobin, or HbA1c, rather than attempting to correct the underlying pathology in the body causing insulin resistance and insulin insufficiency. We believe the current symptom-driven approach to T2D management is misdirected and unreasonable. It asks patients for dietary and lifestyle changes in the face of an altered physiologic set-point in the body, rigorous and lifelong patient adherence and persistence to medicines, and unquestioning willingness to accede to increasingly complex therapies. This burdensome approach to care is often unmanageable and may leave many patients at risk, potentially resulting in chronic elevations in blood glucose that increase the likelihood of microvascular and macrovascular complications of T2D, and even death. There are no therapies that are approved today in T2D that offer disease modification, which we define as ongoing and durable preservation of pancreatic insulin production capacity even after therapy is discontinued.

We believe that recent advances in our understanding of the dysfunction of key metabolic organs now enable the development of new disease-modifying approaches aimed at reversing T2D. Our founders first identified an organ-level pathology of a segment of the intestine, called the duodenum, that may become dysfunctional by the direct impact of modern diets high in fats and sugars. We believe these diets lead to structural and functional pathology of the duodenal mucosa, alter the neurohormonal signal from the gut to the brain and rest of the body, and shift the body's metabolic set-point toward obesity and insulin resistance. Interventions that reduce duodenal nutrient sensing and signaling by a variety of means (such as surgical bypass, endoluminal shunting of food beyond the duodenum, or accelerated nutrient transit through the duodenum after sleeve gastrectomy) have been shown to improve insulin resistance and insufficiency, resulting in lowered HbA1c and reduced risk of developing T2D. Together, we believe these observations help position gut dysfunction as a target for therapy at the apex of the metabolic disease cascade within the body, potentially enabling protection from insulin resistance, obesity and beta cell dysfunction in T2D.

Revita is designed to target the organ-level root cause of T2D in the duodenum with an endoscopic procedure. We believe Revita's unique features can provide a significantly differentiated and compelling solution to the large unmet need in T2D. If successful, we believe Revita could fundamentally disrupt the chronic care model for patients with or at risk for T2D, and could offer the following potential benefits:

- ***Real World Outcomes*.** Revita does not rely on perfect patient adherence or persistence to chronic therapy for its anticipated clinical effects because it is a procedural therapy, unlike diet and lifestyle interventions or pharmacologic management.

- ***Broad Implementation*.** Revita leverages familiar skillsets of advanced endoscopists, can potentially be easily incorporated into endoscopist workflow, fits into most endoscopy suites, typically requires less than five cases for the endoscopist to acquire proficiency, and is designed to be an outpatient procedure that can be performed by a trained therapeutic endoscopist in less than an hour. In addition, in our clinical studies to date, over 95% of endoscopic procedures have successfully ablated the target treatment area.

- ***Patient Friendly*.** Revita is designed to offer a straightforward, outpatient, endoscopic procedural experience for patients, requiring less than a half-day visit, and allowing patients to typically return to their normal daily lives and work the next day.

- ***Significant Health Savings.*** Revita, in combination with at least one ongoing oral antidiabetic agent, or OAD, and lifestyle counseling, has been observed to have a statistically significant mean HbA1c reduction of 1.0% (n=27) and a statistically significant mean fasting plasma glucose, or FPG, reduction of 32 mg/dL (n=28) at 24 months in a long-term follow-up study of the per-protocol, or PP, population in our Revita-1 feasibility study. In addition, Revita, in combination with a glucagon-like peptide-1 receptor agonist and lifestyle counseling, has been observed to help eliminate the need for insulin in eight of 15 patients (statistically significant as compared to baseline) at 18 months in a long-term follow-up study of the PP population in our INSPIRE pilot study. Based on these observations, we believe Revita may help enhance disease control and thereby reduce pharmacological expenditure and improve health outcomes for patients and health systems.

- ***Disease Modification.*** Revita is designed to target and reduce the neurohormonal signal leading to insulin resistance, the underlying metabolic defect of T2D and other metabolic diseases.

- ***Tolerability.*** In clinical studies to date, Revita has been observed to be generally well tolerated, with most patients resuming normal daily activities one day after the procedure and none requiring prescription pain medications. We believe our proprietary SureLift technology enables isolation of the mucosa from deeper tissue structures, sparing pain fibers in the muscle and reducing risk of injury.

- ***Mechanism, Durability, Repeatability.*** Revita is designed to improve metabolic health, blood glucose levels, and weight in patients with inadequately controlled T2D. Based on a long-term follow-up study of the PP population in our Revita-1 study, we observed that Revita, in combination with at least one ongoing OAD and lifestyle counseling, had a statistically significant mean HbA1c reduction of 1.0% (n=27) and a statistically significant raw change in weight of -3.1 kg (n=25) in patients at 24 months. In addition, we believe our SureLift technology has the potential to enable repeat Revita procedures over time. After the commercial launch of Revita, if approved, we may conduct a post-approval study, or PAS, to evaluate the safety and effectiveness of potential repeat procedures, should they be necessary.

- ***Modular System.*** The Revita console is designed to support the duodenal mucosal resurfacing, or DMR, procedure and can also potentially be used to support our Rejuva gene therapy platform, which is designed to provide precise local delivery of gene therapy to the pancreas, in a single endoscopic procedure performed in a single setting.

Revita utilizes a proprietary endoscopic catheter-based approach with control hardware and software with a two-step procedure of (1) thermal isolation of the duodenal mucosa, and then (2) hydrothermal energy delivery to ablate the mucosal surface. The objective of therapy is to disrupt the dysfunctional duodenal neurohormonal signal and allow the rapid regeneration of a new mucosa. To date, Revita has been evaluated in approximately 300 patients across multiple clinical studies and we have observed over 500 patient-years of exposure data across these clinical studies in T2D. In clinical studies of patients with T2D who are inadequately controlled on a variety of antidiabetic agents, or ADAs, we observed the use of Revita, in combination with certain ADAs and lifestyle counseling, lowered HbA1c levels without depending upon additional medication and associated adherence and persistence challenges for patients.

We obtained a Conformitè Europëenne, or CE, mark for Revita in Europe in 2016 for the improvement of glycemic control in patients with inadequately controlled T2D despite oral and/or injectable glucose lowering medications and/or long-acting insulin, although we do not currently market Revita in any territory. In 2022, the Institute for the Hospital Renumeration System (Germany) granted Revita Status 1 designation under its new examination and treatment methods, or NUB, funding process whereby hospitals that submitted a NUB application are now entitled to negotiate reimbursement for the use of Revita in clinical studies and/or real-world evidence generation in a commercial setting. In the United States, we have obtained a Breakthrough Device designation from the U.S. Food and Drug Administration, or the FDA, for Revita in 2021 to perform hydrothermal ablation of the duodenal mucosa, or the Revita DMR Procedure, to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin. Breakthrough Device designation provides certain benefits to device developers, including more interactive and timely communications with FDA staff, use of post-market data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design, and prioritized review of premarket submissions but does not alter or confer any advantage in the regulatory review or approval standard for medical devices. Revitalize-1, which is a pivotal study to evaluate the use of the Revita DMR Procedure in T2D patients who are inadequately controlled with guideline-directed medical therapy inclusive of long-acting insulin, is currently enrolling in the United States and the EU. We have received Investigational Device Exemption, or IDE, approval from the FDA to initiate Revitalize-2, a pivotal study in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy and plan to initiate this study in the second half of 2022. In 2022, we also intend to submit an IDE to the FDA or comparable documents to other regulatory authorities for a clinical study in patients with prediabetes who are at high risk of progression to diabetes, which we refer to as the Revitalize-3 pilot study. If we are successful in developing Revita for certain indications in T2D and prediabetes, we believe Revita could also have the potential to be developed for expanded indications for use in a broader population of patients in other serious diseases, including cardiovascular disease, or CVD, polycystic ovary syndrome, or PCOS, and nonalcoholic fatty liver disease, or NAFLD, among others.

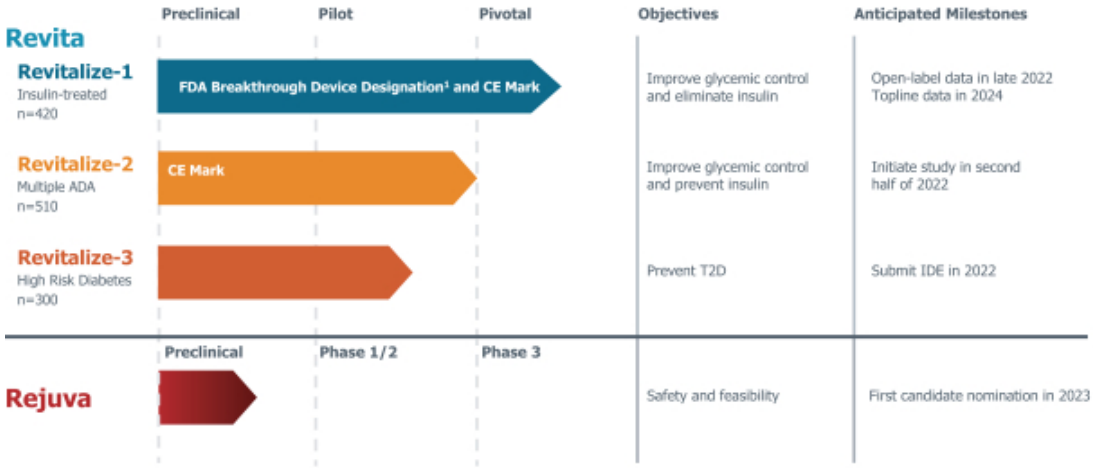
Our novel Rejuva gene therapy platform is designed to restore insulin production capacity in the pancreas via endoscopic, locally delivered adeno-associated virus, or AAV, mediated gene therapy of key metabolic hormones necessary for proper insulin production in the beta cells of the pancreas. Our first gene therapy candidate in the Rejuva program will utilize glucagon-like peptide-1, or GLP-1, receptor analogues. We believe that augmenting GLP-1 receptor activation in the pancreas may lead to reductions in blood glucose through a mechanism distinct from that of the DMR procedure and as an adjunct to Revita. We plan to develop this platform initially for the treatment of advanced, insulin-treated T2D. In a proof-of-concept preclinical study in a diabetic mouse model, we observed a statistically significant average reduction of fasting blood glucose levels of 54% ($p < 0.0001$) and a statistically significant increase in insulin production of 38% ($p < 0.01$) during a glucose tolerance test at a 5-week time point after a single administration of a certain Rejuva platform gene therapy candidate compared to the control vector. No evidence of safety signals to the pancreas or liver were observed in the study. We anticipate nominating our first gene therapy candidate for our Rejuva program and initiating IND-enabling studies in 2023.

We are committed to building the preeminent company focused on developing organ-editing metabolic therapies to treat patients with T2D, leveraging the expertise and capabilities of our team whose singular focus is

on addressing the root causes of the world's leading driver of morbidity and mortality. We envision expanding beyond Revita and our Rejuva gene therapy platform to develop a suite of single-course disease-modifying therapies that comprehensively and robustly address additional independent causes of obesity and metabolic disease. Ultimately, we intend to apply our organ-editing approach to address the metabolic indications that sit at the apex of society's central challenge of obesity and metabolic disease.

Our Development Pipeline

Our development pipeline aims to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. The following table summarizes our development pipeline:



(1) Revita has been granted Breakthrough Device designation to improve glycemic control and eliminate insulin needs in T2D patients inadequately controlled on long-acting insulin; and CE mark obtained in Europe in 2016.

Our Team

We were founded by our Chief Executive Officer, Harith Rajagopalan, M.D., Ph.D., and our Chief Product Officer, Jay D. Caplan, with the goal of developing innovative procedures and novel therapeutics to improve the lives of patients with metabolic diseases, initially targeting T2D. Before starting Fractyl Health, Dr. Rajagopalan was a physician scientist and cardiovascular fellow at Brigham and Women's Hospital. During his M.D./Ph.D. training at Johns Hopkins, Dr. Rajagopalan did award winning research on mechanisms of colorectal cancer formation with significant implications on cancer metabolism and published in leading scientific journals, including *Nature* and *Science*. Dr. Rajagopalan's background in cancer metabolism, cardiovascular medicine and stem cell biology research has contributed to the founding scientific insight behind Fractyl Health: intestinal stem cell biology fundamentally helps to explain one of the root causes of obesity and metabolic disease in humans, along with the attendant health consequences, including T2D, CVD and colorectal cancer. Jay Caplan is an electrical engineer by training and an experienced life sciences executive with an extensive track record of developing transformational medical products, including at ThermoCardio with the development of the HeartMate 2 Left Ventricular Assist Device. Our multi-disciplinary team consists of both seasoned biopharmaceutical and medical device professionals with deep industry experience. Our team brings together experts across multiple areas, including endocrinology (particularly in metabolic diseases), gastroenterology, endoscopy, engineering and medical device development. Members of our team have worked with well-regarded biopharmaceutical and medical technology companies, such as Pfizer, AbbVie and Abbott, and we are supported by a leading group of life sciences investors.

What Sets Us Apart

Our vision is to transform the care of chronic metabolic diseases from the current practice of daily blood glucose management to the treatment of the root causes of T2D and related diseases. Our culture of scientific rigor and innovation is entrenched in all aspects of our organization and informs our goal of disrupting the current inadequate standard of care. While no products that target the gut or the pancreas have been approved, we are focused on developing disease-modifying therapies to treat metabolic diseases by targeting these organs, driving widespread adoption of our novel approach, delivering on the promise of improved experience for patients and health systems, and also potentially reducing costs for the healthcare system. We believe our vision is supported by the following strengths:

- ***Pioneering a New Approach Based on Deep Understanding of Metabolic Diseases.*** Our mission is to pioneer the investigation and understanding of the gut as a root cause of metabolic disease. Our approach builds on over a decade of our research and the accumulation of independently published, supportive clinical evidence from gastric bypass surgeries, all implicating the gut as a validated, untapped target in metabolic disease. We focus our product innovation on targeting the gut and other key organs implicated in the pathogenesis of T2D and related metabolic diseases, with the aim of restoring and preserving the health of the key organs required for metabolic fitness and reducing the burden of metabolic disease for patients and society.

- ***Developing a Disease-Modifying Procedural Therapy for T2D.*** Our lead product candidate, Revita, is designed to disrupt nutrient absorption and address the abnormal neurohormonal signals in the duodenum by targeting and ablating the diseased mucosa in patients with T2D, which has not been attempted previously. In 2021, the FDA granted Revita Breakthrough Device designation, to improve glycemic control and eliminate insulin in T2D patients inadequately controlled on long-acting insulin, which could potentially expedite the development and lead to prioritized FDA review of Revita. Assuming regulatory approval and adoption by key stakeholders, we believe Revita has the potential to address the core weaknesses in the current T2D treatment paradigm and provide long-term clinical benefits to T2D patients by potentially improving overall glycemic control and quality of life while reducing the burden of chronic disease management. Revita is powered by a proprietary balloon catheter and control console, which have been designed with workflow and ease of use in mind to aid with broad commercial adoption by providers and health systems.

- ***Rigorous Approach to Evaluating Revita.*** Our broad clinical program, Revitalize T2D, is designed to advance the development of Revita to potentially become a backbone procedural therapy across the spectrum of T2D. To date, we have evaluated Revita in approximately 300 patients across multiple clinical studies and we have observed over 500 patient-years of exposure data, favorable tolerability data, as well as favorable glycemic control data. The Revitalize T2D program is designed to evaluate our lead product candidate in multiple concurrent clinical studies across a range of T2D patient populations.

- ***Aligning Interests of Key Stakeholders: Patients, Referring Physicians, Providers and Payors.*** We believe Revita, if approved, has the potential to offer clinical and societal benefits while reducing the burden of disease management compared to the current standard of care in T2D. We believe that the successful completion of our clinical studies of Revita, publication of scientific and medical results in peer-reviewed journals, and presentation of data at leading conferences are critical to the clinical and commercial adoption of Revita, if approved. We believe Revita has the potential to broadly align interests across key stakeholders involved in the treatment of T2D, and may have the following benefits to these groups:

    - *Patients.* Improving glycemic control while reducing the number and burden of therapies required to adequately control T2D.

- *Referring Physicians.* Lowering HbA1c for specific patient populations with a procedural therapy, without the escalating need to rely on rigorous patient medication or diet adherence and persistence to medicines, or willingness to accede to increasingly complex and burdensome therapies, ultimately reducing the workload in disease management and improving quality metrics associated with the disease.

- *Providers.* Straightforward, easy to train outpatient procedure, which we believe could be safely deployed at scale across a large patient population. Intended to seamlessly integrate into existing endoscopist workflows and provide a new, profitable service line for hospitals with a patient-friendly therapeutic option for a significant fraction of their patients.

- *Payors.* Significant health economic benefits for payors who are currently struggling with the increasing expenses of T2D, driven primarily by unchecked disease progression and the lack of disease-modifying therapies.

- ***Purpose-Built Leadership Team with Shared Mission to Address Root Cause of Metabolic Diseases.*** Our diverse team, combining marketing, product development and therapeutic expertise, has over 150 years of collective experience in medical devices and biopharmaceuticals. We are mission-driven to develop novel disease-modifying procedural therapies that can potentially reverse metabolic diseases for patients and for health systems. Our team aims to continuously advance and expand upon our body of knowledge in order to establish and maintain a scientific leadership position in our therapeutic areas of focus. We do so by collaborating with expert advisors who are leaders in metabolic disease, endocrine signaling and endoscopy. As part of these ongoing efforts, we have also convened the Erase T2D Task Force, a group of academic and scientific experts in the metabolic disease space, to serve as key advisors as we develop our understanding of the role of the gut in T2D. The Erase T2D Task Force is co-chaired by our CEO, Harith Rajagopalan, M.D., Ph.D., and Alan Cherrington, Ph.D., the former President of the American Diabetes Association and the winner of its Banting Medal for Scientific Achievement.

Growth Strategies

We intend to build a high growth business that is sustainable, predictable and profitable over time. In order to achieve this goal, we plan to employ the following strategies:

- ***Establish Practice-Changing Levels of Evidence Across the Spectrum of T2D.*** Through our Revitalize T2D program, we plan to evaluate the metabolic effects of Revita in approximately 1,000 patients across the disease spectrum of T2D, generating several thousand patient-years of exposure data. Our stepwise approach to regulatory approvals will initially focus on patients with the highest unmet need in T2D, namely those treated with long-acting insulin, and progress to patients in earlier stages of the disease, and patients with high risk prediabetes. In March 2021, we initiated Revitalize-1, a pivotal clinical study of Revita in patients with inadequately controlled T2D despite being on metformin, up to two additional ADAs, and long-acting insulin, and expect topline data in 2024. If successful, we intend to submit a Premarket Approval application, or PMA, to the FDA for Revita to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin. We also plan to initiate Revitalize-2, a pivotal clinical study in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy, in the second half of 2022, and Revitalize-3, a proof-of-concept pilot study in patients with a high risk of prediabetes in 2022. As we execute on the Revitalize T2D program, we believe that the collective data sets generated in these clinical studies, as well as prior clinical studies, will provide comprehensive clinical evidence to support the potential of Revita as a disease-modifying procedural therapy for T2D.

- ***Execute Targeted and Efficient Go-to-Market Strategy.*** If Revita is approved, we plan to execute an efficient “hub-and spoke” commercialization strategy to capitalize on the aligned incentives of key

stakeholders and drive rapid adoption. Leveraging key learnings and insights from the Revitalize T2D program, we plan to assemble a targeted sales force initially focusing on centers of excellence with metabolically focused endocrinologists and advanced therapeutic endoscopists. We plan to initially target participating physicians from our clinical studies, as we believe their familiarity with our product candidate will make them early adopters. Our multi-channel commercialization strategy will include direct marketing campaigns to raise awareness amongst patients for a potential new treatment alternative in advanced T2D. We have begun and will continue to carry out an organized medical education effort to inform endocrinologists around the potential solution provided by our product candidate, as we believe they will serve as the primary prescribing physicians. We will also roll out a robust procedural training and support program for gastrointestinal, or GI, endoscopists, which we believe will ensure seamless integration into their workflow. We believe these educational and training efforts will be critical in building an installed base in metabolic endoscopy that will begin with providers at large hospitals before expanding to outpatient endoscopy centers over time. We also plan to work with Centers for Medicare & Medicaid Services and private insurers to seek to establish coverage and reimbursement for procedures using our product candidate, a key strategy to support the commercial viability of our product candidate with providers.

- ***Expand the Indication and Use of Revita.*** We plan to leverage our platform, technology, core capabilities and the data gathered from our prior clinical studies and the Revitalize T2D program to expand the indication and use of Revita, if approved, within other T2D patient segments, and to potentially further provide a disease-modifying procedural therapy for other serious diseases, including CVD, PCOS and NAFLD, among others. We believe Revita has the potential to impact more than the patient populations and use cases identified in the Revitalize T2D program. Because of our broadly accessible and disease-modifying approach, we intend to expand our focus from improving glycemic control to help enable insulin reduction, elimination, and/or prevention, and ultimately, to become a backbone therapy that can potentially significantly reduce the burden of T2D globally. Additionally, we will pursue incremental product innovation to increase usability and accessibility of Revita. For example, we will explore innovation of the delivery catheters and systems to enable the procedure to be performed in an ambulatory endoscopy setting, rather than in a hospital outpatient setting. Not only would this expand the number of centers in which the procedural therapy can be performed, but would also potentially reduce costs of care as we advance into prediabetes indications and seek to address the global T2D market.

- ***Develop Rejuva Gene Therapy Platform to Enable Long-Term Remission of T2D by Restoring Insulin Production in Patients with Advanced Disease.*** To further our core strategy to treat and significantly reduce the burden of T2D, we are developing the Rejuva gene therapy platform. Our Rejuva platform candidates are being developed as a combination investigational pancreatic delivery device and gene therapy candidates to restore insulin production and metabolic fitness in the pancreas. We believe Rejuva is a first-of-its-kind platform gene therapy program and will potentially bridge a critical therapeutic gap by potentially providing a broadly accessible, disease-modifying therapy for insulin insufficiency. We believe that precise, targeted, low dose administration of gene therapy medicines can address many of the challenges that limit the use of gene therapy in the pancreas today. Rejuva candidates are designed to be locally administered to the pancreas as a single course targeted gene therapy via an endoscopic procedure. We believe Rejuva candidates benefit from localized administration, thereby potentially avoiding the risk of systemic administration, and can be delivered by the same treating physicians and in the same setting as the DMR procedure, using the same console as Revita. Moreover, we believe the metabolic benefits of Rejuva candidates have the potential to be complementary to, and perhaps synergistic with, the Revita DMR Procedure. We plan to nominate our first Rejuva gene therapy candidate for IND-enabling studies in 2023.

- ***Broaden Geographic Footprint for Revita.*** If approved, we aim to commercialize Revita and our other product candidates globally. We obtained a CE mark for Revita in Europe in 2016 and plan to build a direct sales force for distribution in select major European markets. As we expand the adoption of Revita, we will evaluate potential partnerships and/or distributor relationships for its commercialization in other global geographies. Given the high prevalence and rapidly growing incidence of T2D in certain regions, including Africa, India and China, we believe there is a significant unmet need for a scalable, disease-modifying therapy globally. We plan to pursue regulatory approvals and geographic expansion into additional regions as part of our long-term growth strategy.

Our Initial Market Opportunity: Type 2 Diabetes

The cells of our body rely on nutrients from the bloodstream as a source of energy, a process known as metabolism. Glucose, the primary source of energy for cells, must be maintained at certain concentrations in the blood in order to permit optimal cell function and health. Whereas our ancestors lived in and adapted over centuries to ensure adequate energy supply in environments with limited nutrition, most people now live in a modern world with abundant access to calories and levels of nutrition for which we believe our bodies were never designed. Metabolic diseases are a consequence of a multitude of factors, including the genetic-environmental mismatch between our bodies and the abundance of food that the modern world supplies us.

Diabetes mellitus, a disease that can lead to life-threatening problems, affects how the body turns food into energy and disrupts the ability of the body to regulate appropriate levels of glucose in the blood, leading to chronically elevated blood glucose levels. The disease can be caused by the body's inability to produce the hormone insulin, which is produced in the pancreas and regulates glucose levels by helping cells to absorb glucose from the bloodstream, or can be caused by the body's inability to effectively utilize the insulin it produces. The International Diabetes Federation estimates that diabetes currently affects 463 million adults worldwide and contributed at least $760 billion dollars in health expenditure in 2019, a figure that is estimated to grow to more than $2 trillion in global annual expenditure by 2030, according to an independent study by Bommer et al.

Diabetes is typically classified as type 1 or type 2 diabetes.

- **Type 1 diabetes (T1D)** is typically an autoimmune condition characterized by the body's inability to produce insulin due to the inappropriate destruction of insulin-producing cells by the body's own immune system. It affects 5% to 10% of all diabetes patients and is frequently diagnosed during childhood or adolescence. Individuals with T1D require insulin replacement, typically administered via injections or conventional insulin pumps, to survive.

- **Type 2 diabetes (T2D)**, the more common form of diabetes (estimated at 90% to 95% of all diabetes cases), is a metabolic disease associated with the obesity epidemic. It is characterized by the body's inability first to properly utilize insulin and then eventually the body's failure to produce enough insulin. Historically, T2D has occurred in later adulthood, but its incidence is increasing in younger populations due primarily to increasing childhood obesity.

The International Diabetes Federation estimates that nearly 600 million people are expected to be living with T2D globally by 2035. In the United States alone, the CDC estimates that nearly 27 million people have been diagnosed with T2D. A study published by Fang et al. in the New England Journal of Medicine in 2021 reported that glycemic control is worsening in this population and approximately half of these individuals are not achieving targeted disease control despite the availability of over 60 approved drugs for the condition.

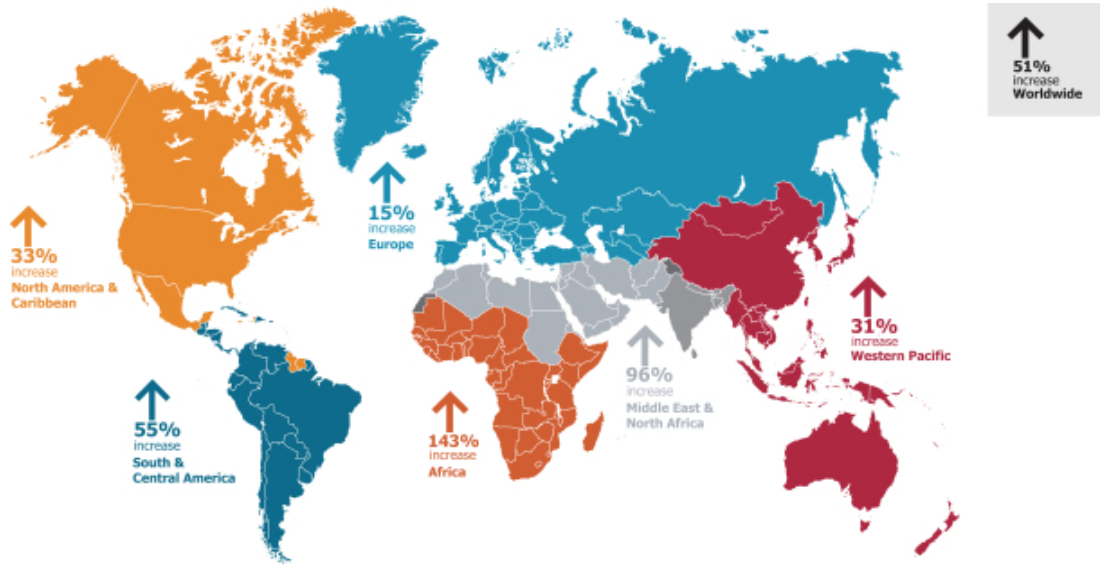
Innovation in T1D has far outpaced T2D in recent years, with new modalities such as cell therapy spurring novel approaches to addressing the underlying root causes of insulin deficiency in the body. Meanwhile, the current standard of care for T2D has stagnated and is driven by life-long symptomatic management, focused on blood glucose control instead of disease modification. This divergence in innovation is evidenced by the lack of practice-changing therapeutics in T2D, and despite the fact that T2D affects a significant fraction of the global

population, there has not been a novel mechanism of action introduced to treat T2D in over a decade and there are no approved disease-modifying therapies that target the organ-level root causes of the disease today.

Type 2 Diabetes Overview

Modern changes in diet and lifestyle have led to an increase in obesity and associated metabolic diseases around the globe and have become a principal driver of morbidity and mortality in the 21st century. As a significant part of this increase, the T2D epidemic is global and growing. The below image, based on data from the International Diabetes Federation, depicts the projected rapid growth of diabetes from 2019 to 2045.

Global Prevalence of Diabetes is Growing at an Alarming Rate

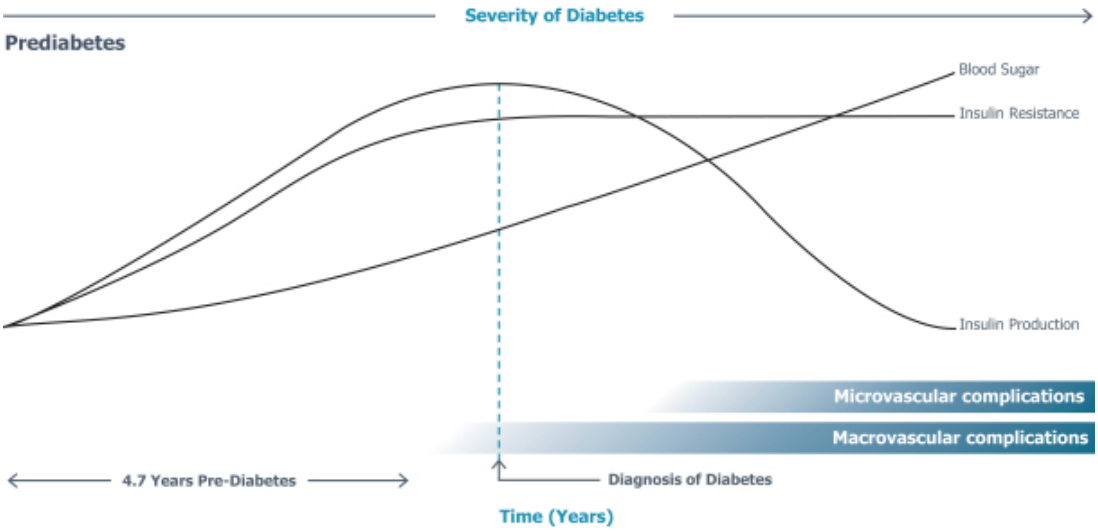


T2D is a disorder of rising blood glucose that is caused by a multitude of factors, which lead to two parallel, progressive disease processes within the body: insulin resistance and insulin insufficiency:

- **Insulin resistance** is the body's inability to appropriately utilize an insulin signal from the pancreas to remove glucose from the bloodstream. The resistance to insulin causes excessive glucose production in the liver and a chronic strain on the insulin producing beta cells of the pancreas, which ultimately leads to insulin insufficiency. The systemic metabolic dysfunction associated with insulin resistance is not limited to the pancreas. Insulin resistance is also associated with systemic chronic inflammation and other negative consequences throughout the body independent of blood glucose that can lead to disease, including in the liver, cardiovascular system, and brain.

- **Insulin insufficiency** in T2D is the gradual failure of the beta cells to produce sufficient insulin to meet the body's needs. Early on, an individual's genetic makeup and the gradual impact of diets high in fat and sugar lead to insulin resistance, requiring the pancreas initially to chronically overproduce insulin in order to maintain control of blood glucose within a normal range. Over time, both the stress of insulin resistance and the exhaustion of excessive insulin production can cause the progressive failure of beta cells and a decline in insulin production. This combination of insulin resistance and consequent progressive pancreatic failure results in high blood glucose levels.

Insulin Resistance and Insulin Insufficiency Drive Higher Blood Glucose Levels



Insulin resistance occurs relatively early in life and at first is not associated with elevated blood glucose but does contribute to systemic chronic inflammation and the risk of CVD and stroke even without elevations in blood glucose. Over time, insulin resistance causes a strain on pancreatic insulin production. Patients with prediabetes have insulin production that has reached maximal levels (significantly higher than in those without diabetes) and yet is still insufficient to overcome the resistance to insulin action throughout the body. Prediabetes is often diagnosed by the elevated blood glucose that ensues and can be measured in either the fasting state or two hours after a fixed dose of glucose. Currently there are no FDA-approved therapies for prediabetes and most society guidelines focus only on diet and lifestyle recommendations, even though prediabetes is already an indication of pancreatic dysfunction. The CDC estimates that there are approximately 88 million adults with prediabetes in the United States, and that nearly 40% of patients with prediabetes will progress to diabetes in their lifetimes, with 20 million expected to be diagnosed with T2D by 2035. This occurs as pancreatic insulin production progressively declines and blood glucose begins to rise inexorably.

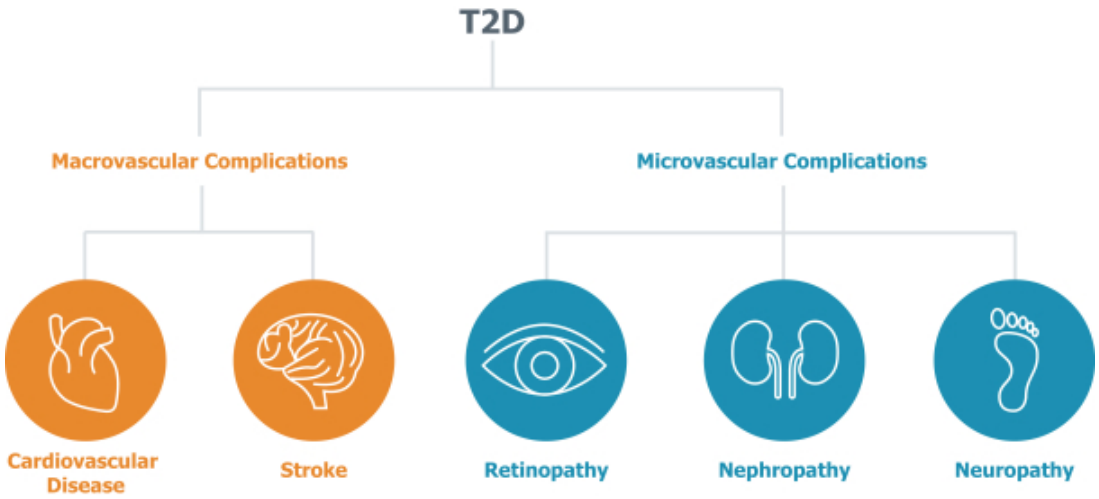
When worsening pancreatic function leads to rising blood glucose above certain defined cutoff values for the population, the diagnosis of diabetes is made. Diabetes can be diagnosed by a FPG (plasma glucose measured after at least 8 hours of fasting), above 126 mg/dL or a blood glucose above 200 mg/dL, measured two hours after a glucose tolerance test. A HbA1c test can also be performed without the need for a fasting measurement of glucose tolerance test because it measures average blood glucose over a period of the past two to three months. Prediabetes is often diagnosed at HbA1c levels between 5.7% and 6.4% and diabetes is diagnosed when HbA1c reaches 6.5% or higher. Most society guidelines focus on controlling blood glucose to levels less than or equal to 7%, below which risk of diabetes related complications is low.

Controlling Blood Glucose—Benefits and Challenges

High cumulative life-long exposure to blood glucose in diabetes drives the development of diseases associated with small blood vessels (e.g., microvascular diseases in the eye, kidney, and peripheral nerves) and large blood vessels (e.g., macrovascular diseases in the heart and brain), potentially leading to life-threatening complications throughout the body, including early mortality. According to the National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, T2D retinopathy is the most common cause of adult blindness in the United States, affecting an estimated 40,000 U.S. patients each year; diabetic nephropathy is the most common cause of kidney failure in the United States, affecting an estimated 58,000 U.S. patients each year; and T2D

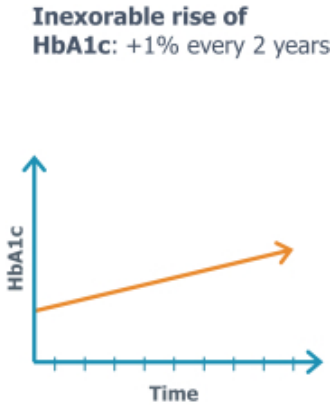
neuropathy is the most common cause of atraumatic amputation in the United States, affecting an estimated 100,000 U.S. patients each year. In addition, T2D is a major risk factor for cardiovascular events, such as heart attack and stroke. Ultimately, the mortality risk for patients with T2D is a nearly 2-fold higher than in people without the disease, mainly due to cardiovascular complications of the disease.

Macrovascular and Microvascular Complications of T2D



The relationship between the lowering of cumulative blood glucose exposure (HbA1c – a validated measure of blood glucose control) to normal levels and reduction in the risk of microvascular and macrovascular disease is among the longest and best understood relationships in medicine. HbA1c reflects average levels of blood glucose over the previous two to three months and is the most widely used clinical test to estimate mean blood glucose and monitor glycemic control. HbA1c is used by clinicians to diagnose diabetes and to monitor the efficacy of diabetes treatment. Large scale epidemiologic studies have shown that a 1% lowering of HbA1c lowers the overall risk of microvascular complications by approximately 35%. This demonstrates that the challenge is not only to substantially reduce HbA1c but also to sustain such a reduction throughout a patient's lifetime.

T2D is a Progressive Disease Characterized by Worsening HbA1c Levels

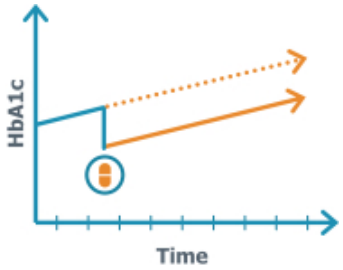


Current Treatment Paradigm

The standard initial therapy in T2D is preventative care: dietary and lifestyle interventions aimed at altering the risk factors that contribute to progression of disease. While alterations to lifestyle are important, even intensive diets have not demonstrated sufficiently durable effectiveness to favorably impact long-term health in most patients due to lack of persistence and adherence. The Look AHEAD trial, conducted by the NIDDK, was a randomized controlled trial comparing an intensive lifestyle program to standard diabetes education in overweight and obese T2D patients to track the development of CVD over time. The trial was stopped for futility after a median follow-up of 9.6 years. There was a differential effect of intensive lifestyle intervention on weight loss and fitness for some period of time but there was no effect of dieting on cardiovascular outcomes as compared to the group that received diabetes support and education. One reason for the challenge of lifestyle interventions is that obesity alters the body's physiologic set-point, leading the body to abnormally try to defend its high weight through the hunger people typically experience while dieting. Eventually, even with diet and lifestyle interventions, blood glucose often worsens as ongoing insulin resistance causes progressive failure of pancreatic beta cells. At this point, symptomatic therapy to manage hyperglycemia is needed and most patients advance to medications and the chronic-care therapeutic model we see today.

The first prescription of an OAD is almost always metformin, the most highly prescribed drug in the world. Most patients with T2D will remain on metformin throughout their lives. Several other classes of oral drugs also exist for the management of hyperglycemia, and the sequential addition of medication on top of metformin is directed by patient preference and payor pressure to minimize costs. The sodium-glucose cotransporter-2 inhibitor, or SGLT2i (e.g., empagliflozin), and GLP-1ra (e.g., semaglutide), classes emerged over ten years ago as important new therapies in T2D with benefits beyond glucose lowering alone, including broader metabolic benefits on cardiovascular and kidney disease risk. Guidelines call for patients to typically try SGLT2i and GLP-1ra if affordable before progressing to insulin therapy, helping to make the SGLT2i class an estimated $7 billion market and the GLP-1ra class an estimated $12 billion market in 2020. The significant market uptake of these drugs has come despite important shortcomings. SGLT2i and GLP-1ra medicines have a black box warning associated with significant safety risks, as well as tolerability challenges affecting medication adherence. Since the introduction of these two classes over 10 years ago, there have been no significant new targets or approaches in the T2D disease category.

Medical Therapies Lower Blood Glucose but do not Alter the Rate of Progression



Eventually, medications lose durable effectiveness in the face of ongoing diabetes progression, and most patients typically progress to insulin therapy if they do not achieve suitable control on two or three ADAs. Most patients start with long-acting insulin, a daily injectable therapy, which lowers blood glucose by suppressing liver glucose production and helping cells absorb glucose from the bloodstream.

Insulin is a very effective drug at lowering blood glucose in controlled clinical trials but presents significant limitations as a sustainable therapy, as evidenced by unfavorable real world outcomes with this class of medicines. Despite its potency, fewer than 40% of patients achieve good glycemic control even after long-acting insulin is added to their regimen because of a failure on the part of patients and physicians to titrate insulin

dose appropriately and a lack of adherence or persistence on therapy in many patients. Insulin has several problems that prevent it from achieving better glycemic control in the real world, outside of clinical trials, including:

1. Insulin carries significant side effects of weight gain and hypoglycemia that are proportional to the amount of insulin that a patient administers;

2. Insulin requires daily blood glucose monitoring and prevention of hypoglycemia, which places a considerable management burden on patients;

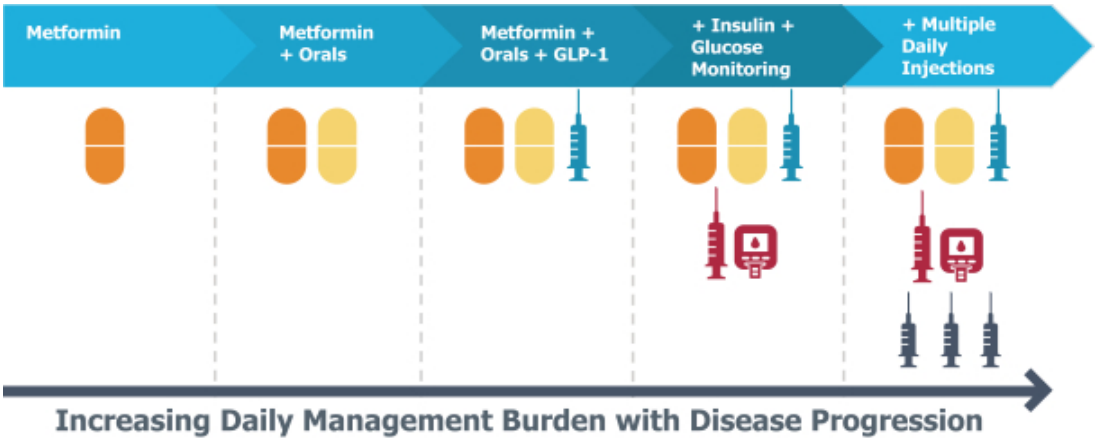
3. Insulin does not curb the progressive worsening of blood glucose, leading patients to be forced to increase their daily insulin by 9 to 10 units/day annually in order to maintain the same level of glucose control as the body's own insulin production continues to worsen;

4. Insulin has a ceiling effect above doses of approximately 0.5 u/kg/day (approximately 50 to 60 units per day in an average patient), above which side effects continue to increase but glucose lowering has diminishing benefit;

5. Insulin carries a social stigma associated with a sense of failure and lack of other options at the end of the line of diabetes care; and

6. Insulin has seen a 850% price increase over the last ten years without any change to the mechanism, limiting accessibility for patients and hampering consistent use.

Failure to achieve blood glucose control with metformin, other ADAs, and even long-acting insulin leads to the need for more intensive insulin therapy with multiple daily injections of insulin each day, including long-acting and short-acting insulin formulations, or even to insulin pump therapy. This rigorous routine is a massive burden on patients, leading to decreased adherence, and ultimately, resistance towards therapy. The chart below shows the cumulative medication and disease management burden on patients associated with the progression of T2D.



Limitations of the Current Treatment Paradigm

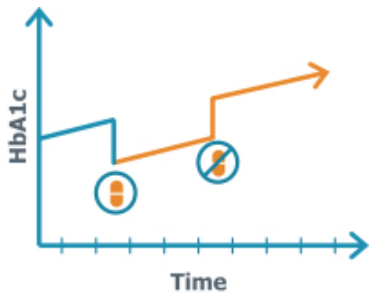
Guidelines today focus on managing the blood glucose symptoms of T2D, often measured by HbA1c, rather than attempting to correct the underlying pathology in the body causing insulin resistance and insulin insufficiency. We believe the current symptom-driven approach to T2D management is misdirected and

unreasonable. It asks patients for dietary and lifestyle changes in the face of an altered physiologic set-point in the body, rigorous and lifelong patient adherence and persistence to medicines, and unquestioning willingness to accede to increasingly complex therapies. This burdensome approach to care is often unmanageable and may leave many patients at risk, potentially resulting in chronic elevations in blood glucose that increase the likelihood of microvascular and macrovascular complications of T2D, and even death. There are no therapies that are approved today in T2D that offer disease modification, which we define as ongoing and durable preservation of pancreatic insulin production capacity even after therapy is discontinued.

A principal challenge of maintaining appropriate blood glucose control over time is that T2D is a progressive disease, characterized by the steady and progressive loss of pancreatic beta cell function over time caused mainly by insulin resistance and consequent insulin insufficiency. Instead, we believe the current standard of care is a chronic care model that actually enables and accelerates the progressive deterioration of pancreatic function because it focuses on blood glucose control (i.e., symptom management) while failing to prioritize efforts to curb the upstream insulin resistance and the downstream impact on the beta cells that is causing insulin production to fail. In fact, the American Diabetes Association guidelines only call for medication escalation when blood glucose is already high and pancreatic beta cell failure has already advanced (i.e., when HbA1c rises above 7%) and ongoing beta cell failure has already manifest.

Furthermore, given the silent nature of the damage done by elevated HbA1c, many patients at risk for T2D do not properly appreciate the therapeutic benefits of consistent treatment or the substantial risk of foregoing treatment. Many patients focus instead on the burden of heavy, escalating, life-long medication requirement from pills and injections, requisite diet and lifestyle changes and other chronic glucose monitoring and management approaches. As a result of this treatment burden, many patients do not titrate therapy once prescribed, adhere to therapy consistently, or persist on prescribed therapy in T2D for a long enough period of time to achieve clinical benefit from them. In fact, the proportion of patients who persist with even the most effective therapies, such as the GLP-1ra class, remains at only approximately 55% at 12 months even though they are weekly injectable therapies designed to improve adherence. Because ADAs do not alter the underlying pathology of disease, treatment discontinuation often results in patients returning to their prior trajectory and rate of disease progression.

Discontinuation of Medicines Returns Patients to Prior Trajectory of Disease



These challenges are particularly acute at the transition to insulin therapy, where the lack of appropriate titration, adherence, and persistence is particularly problematic. In addition, inertia on the part of patients and physicians often delays treatment escalation to insulin for most patients for up to three years because of the undesirability of insulin. For these reasons, we believe the current chronic care model of management inevitably leads a large proportion of patients with established T2D to have unacceptably high HbA1c levels.

We believe that single-course, long-duration therapies that potently and durably control cumulative HbA1c exposure in a manner that slows the rate of disease progression could fundamentally disrupt the chronic care model for patients with or at risk for T2D and relieve the significant burden placed on patients, providers

and the healthcare system. We believe there is a significant unmet need for disease-modifying therapies that reduce daily disease management burden and have the potential for broad accessibility in the large and growing T2D market.

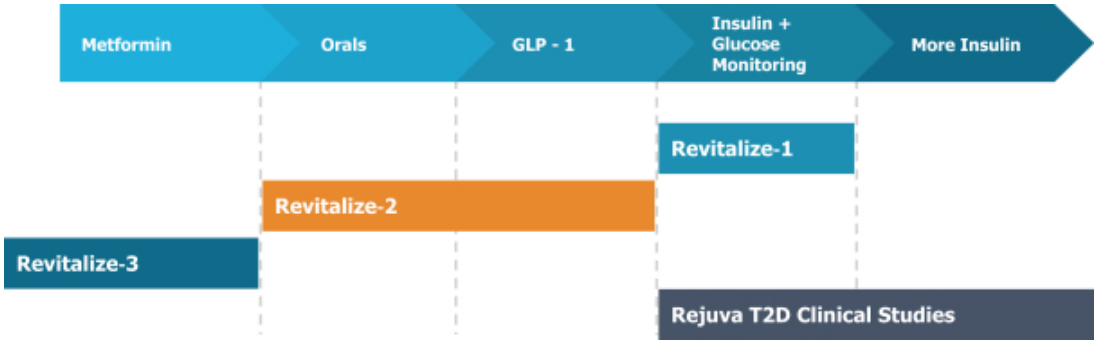
Our Solutions

We are seeking to create new solutions that address the therapeutic gaps in the current T2D treatment paradigm by designing disease-modifying therapies that are easy to administer and broadly accessible. We believe that our product candidates have the potential to address the most prominent shortcomings that are inherent in the current standards of treatment for T2D. Lifestyle and dietary management solutions suffer from practical and unavoidable challenges related to adherence. Existing ADAs focus on managing blood glucose symptoms of T2D (i.e., HbA1c), pose a significant economic burden, and require lifelong adherence and persistence for effectiveness. We believe our product candidates are intuitive to administer, can be completed in an outpatient procedure in less than one hour, and can be delivered in a broadly accessible and cost-effective manner to achieve clinical benefits that have the potential to be durable and to reduce disease burden in society.

We believe that the focus of care in T2D should transition from symptomatic therapies aimed at lowering HbA1c to disease-modifying approaches aimed at correcting the underlying pathology in the body causing insulin resistance and insulin insufficiency. In order to be maximally impactful, these therapies must also be delivered at a scale that can match the incidence and prevalence of T2D around the world. We believe our product candidates have the capacity to revolutionize treatment of T2D and, at their fullest potential, to significantly reduce the burden of metabolic disease globally.

We are developing a suite of product candidates that will target T2D at all phases of the disease – from prediabetes to insulin-treated T2D and, eventually, to late-stage T2D requiring advanced insulin therapy. Our Revitalize T2D program is designed to evaluate Revita in multiple concurrent clinical studies across a range of patient populations from prediabetes to T2D patients on long-acting insulin. Additionally, we are developing a novel pancreatic gene therapy platform, Rejuva, to enable long-term remission of T2D by potentially restoring insulin production in patients with advanced disease.

Revitalize and Rejuva T2D Clinical Studies Span Entire T2D Spectrum



Our Approach

Our approach rests on designing disease-modifying procedural therapies that precisely target and alter the function of the diseased organs responsible for two of the root causes of T2D: insulin resistance and insulin insufficiency.

Revita: Our lead clinical product candidate, Revita, is designed to target the dysfunctional duodenal mucosa, which is a driver of the underlying insulin resistance of T2D. Revita is designed to improve insulin

sensitivity in the body, which can reduce the amount of insulin required to control blood glucose and ease the strain on the pancreas in order to slow the progressive decline of beta cell function that is the hallmark of T2D. We believe Revita accomplishes this through a minimally invasive endoscopic procedural therapy that isolates the mucosa from the deeper muscle layer of the duodenum, which we refer to as our SureLift technology, and hydrothermally ablates the excess layers of the duodenal lining with a proprietary balloon catheter and control console. In the days following the ablation procedure, the duodenal mucosa regenerates, which we believe leaves the duodenal lining revitalized and better able to properly coordinate the gut's metabolic signaling pathways in a manner that potentially improves insulin sensitivity.

Revita is being designed to treat patients with inadequately controlled T2D who have not yet lost insulin production capacity in their pancreas—ranging from prediabetes to those on long-acting insulin but not yet requiring multiple daily injections of insulin. For individuals with prediabetes, Revita is designed to improve insulin sensitivity to reduce the strain on the pancreas, and thereby potentially prevent substantial deterioration of pancreatic function. For people with early stage T2D treated with medicines and up to the point where they require multiple units of long-acting insulin, Revita is intended to improve glucose control and reduce the need for insulin therapy. However, Revita as a standalone therapy is not intended for patients with T2D whose beta cell function is severely impaired. We are intending to treat this latter patient population with our gene therapy platform—Rejuva.

Rejuva: Our novel gene therapy platform, Rejuva, consists of gene therapy candidates that are being developed as combination investigational pancreatic delivery device and gene therapy candidates to target the dysfunctional pancreatic beta cells that are a root cause of insulin insufficiency in T2D. Rejuva is being designed to directly administer a gene therapy into the pancreas to potentially restore insulin production capacity in the pancreatic beta cells, thereby potentially recovering the function of an organ that had been damaged by T2D progression. Our Rejuva platform candidates are being developed to accomplish this through a minimally invasive, endoscopic procedural therapy that delivers an AAV vector carrying a transgene that potentially enables the local production of hormones in the pancreas that are necessary for insulin production. These hormones are intended to rejuvenate beta cell health and restore the body's natural ability to produce insulin. The first gene therapy candidate for Rejuva will be a GLP-1 receptor analogue transgene that expresses a GLP-1 hormone within the pancreatic beta cells and secretes this hormone into the surrounding pancreatic islets.

By employing Revita and Rejuva to potentially address both insulin resistance and insulin insufficiency, we believe it is possible to remedy the core pathologies underlying T2D. If we are able to obtain approval for these product candidates, we believe these therapies will allow us to chart a course towards significantly reducing the burden of T2D globally.

Our Targets

"All disease begins in the gut."

- *Hippocrates*

The Role of the Gut in the Central Regulation of Metabolism

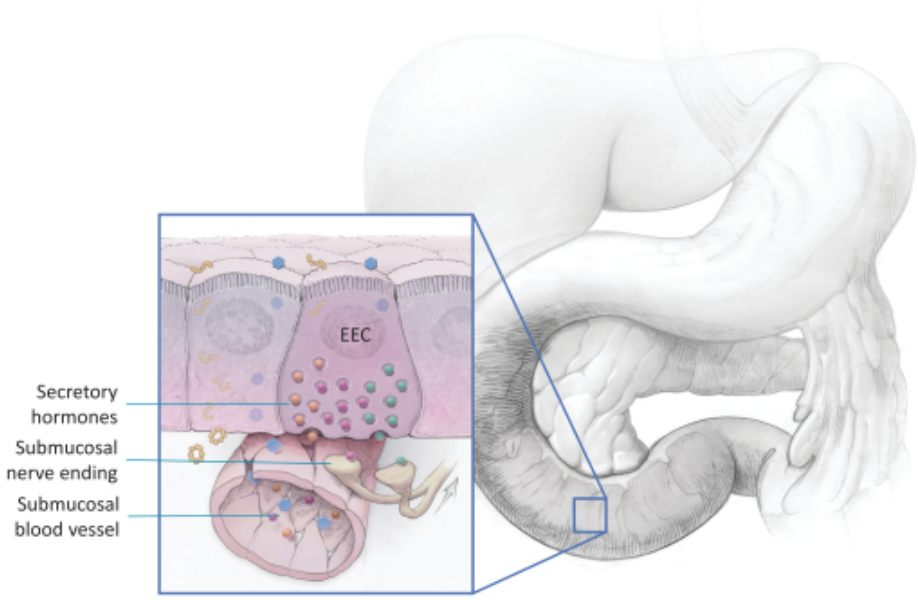
In recent years, there has been an increase in research tying gut health to diseases throughout the body – ranging from obesity to T2D to dementia. One aspect of this research is the increasing recognition that an important root cause of metabolic disease is the impact of modern diets on the gut, one of our body's critical metabolic control systems. Advances in our understanding of integrative organ physiology has begun to reveal the complex role that the gut plays in interfacing with the food we eat and coordinating the body's response to that food. The gut possesses the largest nervous system outside the brain, the largest hormone producing endocrine system, a huge and complex microbiome, and the largest immune system in the body. Different segments of the intestine have different endocrine producing cells and different neurohormonal effects on the brain's response to the meal. These mechanisms work together to provide a defensive barrier and an early warning detection system to help the body prepare for and deal with the food we ingest.

Diets have changed a great deal over the past several decades, with a shift away from relatively calorie poor, fiber rich, natural foods, to the inexpensive and abundant supply of ultra-processed foods that are very high in simple fats and sugars. Our founders, along with several scientific groups around the world, have begun to detail the specific changes that these modern diets cause on the gut and the impact these changes exert on the body and brain. While the gut has long been recognized as an acute nutrient sensor with signaling mechanisms to the other metabolic organs of the body, its role in regulating the body's metabolic status over longer periods of time has been underappreciated. Recent advances have demonstrated that the chronic exposure of the intestine to high levels of fats and sugars may lead to structural and functional changes of the lining of the proximal gut that signal a metabolic shift to the brain and body. These insights provide a window into the adaptive role of the intestinal mucosa in helping to define metabolic parameters within the body—informing the metabolic regulation of insulin resistance versus sensitivity, hunger versus satiety, energy utilization versus energy storage, and protection from hypoglycemia versus protection from hyperglycemia. Moreover, these diet-induced changes are geographically confined to the upper small intestine, particularly the duodenum, an area of the body that is directly accessible via routine upper endoscopy via the mouth. This new research now provides, for the first time, an accessible potential target of pathology within the gut that sits at the apex of the complex metabolic changes throughout the body underlying both obesity and metabolic disease.

Structural and functional changes in the duodenal lining occur in insulin resistant patients

After food passes through the stomach, it moves to the duodenum, which is the first approximately 25 cm to 30 cm of the small intestine, where nutrient absorption first begins in the body. The lining of the duodenum, known as the mucosa, is composed of several cell types, including absorptive cells called enterocytes and hormone-producing enteroendocrine cells, or EECs (comprising approximately 1% of the cells of the mucosa). EECs sense the presence or absence of nutrients in the duodenum and send chemical signals via the bloodstream and direct connections to nerve cells in the gut to the brain and body to help mediate glucose control, as depicted below.

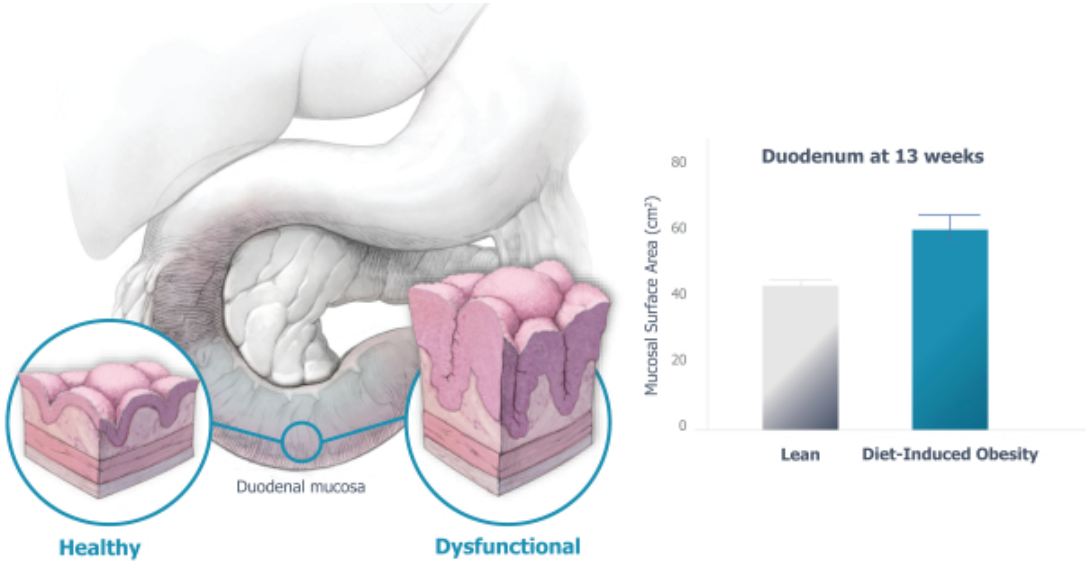
EECs in Duodenal Lining Send Neurohormonal Signals to Brain and Body



Studies analyzing the small intestine in diabetic patients and animal models have identified mucosal abnormalities after chronic dietary exposure to high concentrations of fat and sugar similar to the composition of

modern diets. Geltrude Mingrone (who has become a consultant to Fractyl and a member of our Scientific Advisory Board), et al. showed in 2010 that a high fat diet in rats can cause overgrowth of the duodenal mucosa. Working with colleagues at King's College London, we extended these observations to show that mucosal overgrowth may occur in the duodenum and proximal jejunum but does not extend to further segments of the intestine, such as the ileum. Further, we observed a diet-induced response of stem cells dividing more rapidly at the base of the duodenum due to high concentrations of fat and sugar, which led to an overgrowth (i.e., hyperplasia) of the duodenal mucosa. The figure on the left demonstrates that chronic exposure to these diets may lead to the development of a dysfunctional duodenal lining. The image below on the right depicts the effect of a high fat diet on the growth of the mucosa in a rodent chronically fed a high fat diet, which led to a 50% increase in mucosal surface area over time, relative to a normal diet-fed rodent.

High Fat and Sugar Diets May Cause Overgrowth and Dysfunction of Duodenal Mucosa



This finding of a nutrient-induced stem cell division process that causes structural and functional changes of the duodenal mucosa has now been replicated by multiple independent groups in the United States and Europe, and across organism species and disease models. Michael Theodorakis et al. have demonstrated similar observations in diabetic humans, showing through duodenal biopsies that the mucosa in the duodenum of patients with T2D becomes thickened and exhibits changes to the hormone-producing cell populations in the duodenum.

Hyperplasia and dysfunction of the duodenum is associated with more mucosal cells, a greater surface area for nutrient absorption, and in turn more EECs for neurohormonal signaling, altering the body's response to the metabolic signal from this region of the gut. The greater surface area of the duodenal lining accelerates nutrient absorption and nutrient sensing and signaling from EECs in the proximal intestine. Multiple downstream mechanisms have been implicated in the role of this gut dysfunction in causing insulin resistance: increased glucose-dependent insulinotropic polypeptide hormone secretion, altered gut permeability, increased iron absorption, altered gut-brain signals, bile acid changes, and microbiome alterations have all been invoked as potential mediators of insulin resistance from the gut. In addition, the shift in nutrient absorption toward the proximal intestine effectively reduces nutrient signaling and absorption in the distal intestine. Less nutrient sensing in the distal intestine then reduces the secretion of key gut hormones from the distal intestine (e.g., GLP-1 and peptide YY, or PYY) that are known to improve insulin sensitivity and satiety. Scientists have shown

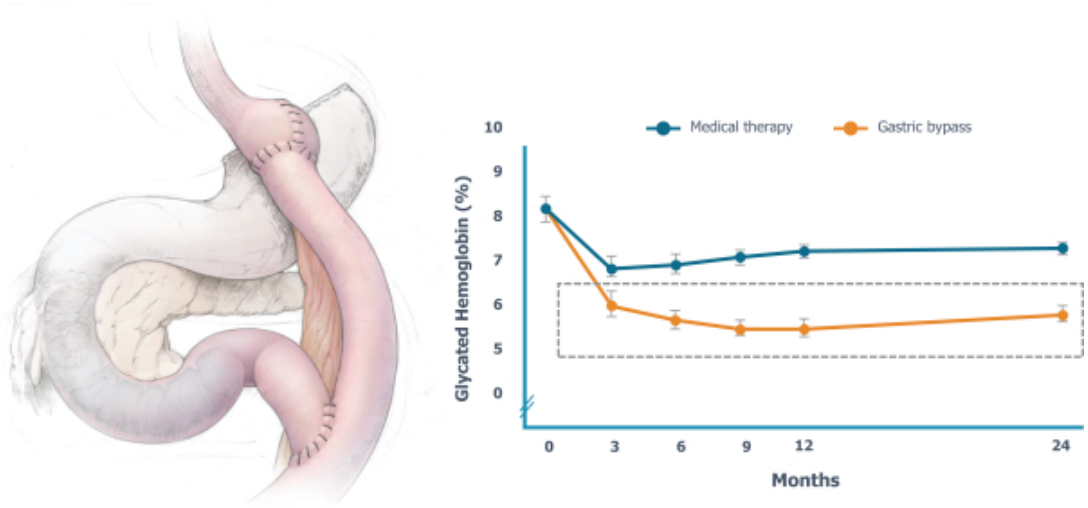
that patients with T2D and obesity have decreased secretion of GLP-1 and PYY from the distal intestine, and that this impairment of GLP-1 and PYY release may further contribute to the hunger and hyperglycemia of T2D.

We believe that, taken together, this recent preclinical and clinical evidence demonstrates that abnormal neurohormonal signaling from the duodenum to the rest of the body is an important contributor to insulin resistance in patients with T2D. This insight extends the conventional wisdom that excess weight and physical inactivity are the sole drivers of T2D by highlighting the important role of the duodenum in insulin resistance.

Avoiding Nutrient Contact with the Duodenum can Reduce Insulin Resistance in T2D

Not only is there evidence that changes in the duodenum and duodenal nutrient sensing may directly and/or indirectly cause insulin resistance, but independent studies in animals and humans show that preventing or disrupting nutrient contact with the duodenal mucosa can ameliorate insulin resistance and its downstream clinical consequences. Metabolic surgeries that bypass the stomach and duodenum, originally intended for weight loss, have emerged as a treatment approach in T2D with superior metabolic benefits compared to the current standard of care. There is abundant and compelling surgical experience (performed in hundreds of thousands of patients with millions of patient-years of follow-up) showing significant and durable metabolic improvements that come from bypassing the duodenum in people with obesity and T2D (as depicted in the image below).

Gastric Bypass Surgery Leads to Significant and Sustained Improvement in Blood Glucose

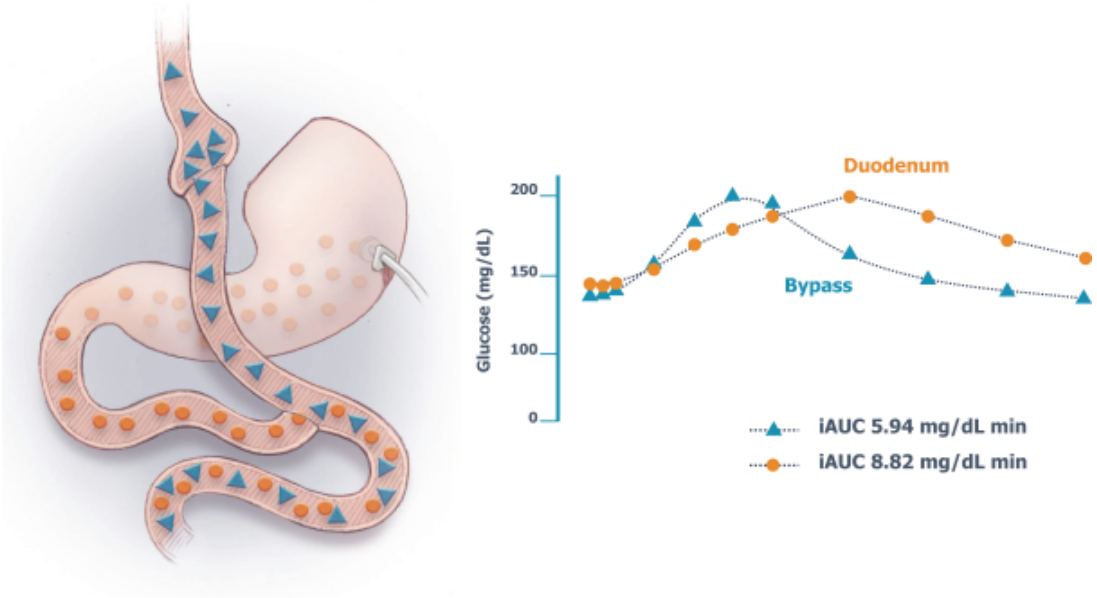


Source: Mingrone et al., *N Engl J Med* 2012; 366:1577-1585

These surgeries have now firmly positioned the duodenum as a validated novel target for T2D and an organ whose function can be safely and effectively altered for metabolic improvement. Many of the metabolic improvements occur independently of weight loss and appear to be related to disrupting nutrient contact with the duodenum. In rat models of T2D, bypass of the duodenum has demonstrated improvement in insulin sensitivity, a reduction in fasting glucose levels, and protection from weight gain even when animals are exposed to a high fat diet. In humans and rats, an intestinal implant that prevents nutrients from contacting the duodenal mucosa also demonstrated a similar improvement in insulin resistance and fasting glucose. People who incidentally undergo a duodenal bypass to treat other conditions appear to be protected from the development of T2D.

While gastric bypass surgeries that exclude the duodenum have demonstrated improved glucose tolerance, reversal of the bypass and restoration of duodenal nutrient contact has shown glucose levels to worsen again almost immediately. The image below depicts the effect of food on glucose control when the food passes through the duodenum versus food bypassing the duodenum in the same individual on successive days. Dirksen et al. showed that the average blood glucose after a meal is 34% higher (i.e. more diabetic) when food is delivered via the duodenum versus when the duodenum is bypassed (as depicted in the image below).

Bypassing Duodenum Leads to Immediate and Weight Independent Improvement of Blood Glucose



Source: Dirsken et al., *Diabetes Care* 2010 Feb; 33(2): 375-377

We believe the most profound impact of bariatric surgery is that it provides a powerful new idea of how to tackle the underlying root causes of metabolic disease and a target for new therapies. The surgery teaches that the location of nutrient delivery within the gut is potentially more important than the nutrient itself. While a normal diet can lead to normal signaling patterns from the foregut and hindgut to the rest of the body, years of consistent exposure to calorie-dense diets can potentially lead to hypertrophy of the foregut. We believe these conditions lead to a preponderance of EECs and can cause abnormal signaling patterns to emerge. Recent evidence has demonstrated that these abnormal signaling patterns potentially lead to T2D.

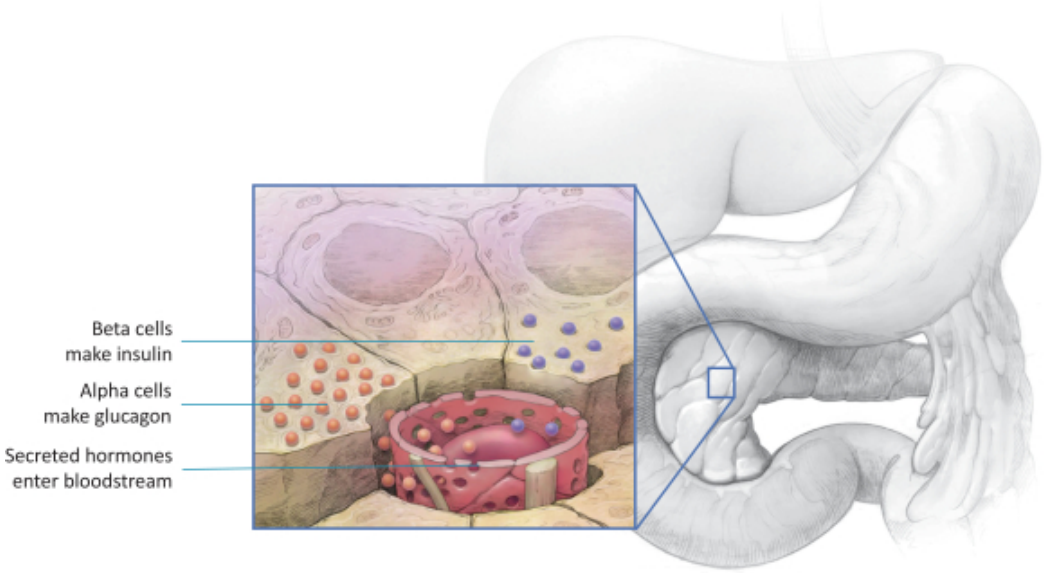
Instead of an invasive surgery to bypass the duodenum, we believe it is possible now to understand the role of the mucosa of the duodenum as a critical but diseased segment of the intestine whose nutrient sensing and signaling abnormalities potentially cause the brain and body to develop insulin resistance and metabolic dysfunction. The surgery provides a serendipitous insight into the duodenal mucosa as a target for disease-modifying therapies which, unlike gastric bypass, does not require an invasive surgery, and unlike lifestyle interventions or ADAs, does not require adherence and persistence to achieve clinical benefit.

The Role of the Pancreas in Insulin Insufficiency

The pancreas is a hormone producing organ in the retroperitoneum surrounded by the duodenum, immediately below the stomach. It has functions related to the secretion of digestive enzymes into the duodenum

to help process food for absorption (exocrine pancreas) and functions related to the secretion of hormones into the bloodstream to help maintain glucose control (including insulin and glucagon) from pancreatic islets distributed throughout the pancreas. The figure below shows cells within a pancreatic islet: alpha cells secrete glucagon into the bloodstream and beta cells secrete insulin. Glucagon and insulin are counter-regulatory hormones that act in opposite directions to raise or lower blood glucose levels, respectively.

Pancreatic Islet Cells Produce Glucagon and Insulin



Most people can compensate for their bodies' insulin resistance by increasing the amount of insulin they produce in the beta cells of their pancreas. Patients who go on to develop T2D eventually experience a gradual loss of insulin production over the course of many years. By the time that the diagnosis of diabetes is made, people have lost over 80% of their beta cell function, which we believe makes it essential that the physician intervene aggressively with therapies known to correct known pathophysiological disturbances in beta cell function. There are two principal causes for the loss of beta cell function in most people with T2D: (1) exhaustion of beta cell function in the face of longstanding insulin resistance and chronically elevated blood glucose levels, (2) damage to beta cells from the toxicity of circulating lipids (i.e., lipotoxicity) that are directly tied to insulin resistance.

Increasing GLP-1 Levels in the Pancreas can Improve Insulin Production

GLP-1 is a potent hormone that is predominantly produced in the distal intestine and secreted into the body by distal intestinal EECs in response to nutrient intake, leading to a rapid rise in circulating GLP-1 after a meal. The role of GLP-1 hormone in beta cell function and insulin production is one of the best understood hormonal mechanisms in all of medicine. The GLP-1 receptor is expressed in beta cells of the pancreas, where receptor activation has multiple acute and chronic actions on beta cell function: acutely, GLP-1 immediately stimulates insulin secretion in response to elevations in blood glucose (glucose-stimulated insulin secretion); chronically, GLP-1 stimulates insulin gene transcription and islet cell survival. The GLP-1 receptor is also expressed in alpha cells of the pancreas, where receptor activation regulates glucagon expression in order to help control blood glucose levels. Taken together, the beneficial effects of GLP-1 on pancreatic islet function have been further demonstrated by the effects of the GLP-1ra class of medicines, which have demonstrated meaningful improvements in insulin production and pancreatic responsiveness to blood glucose.

Revita and Rejuva are designed to treat insulin resistance and insulin insufficiency by directly targeting the gut and pancreas, respectively, to restore the body's natural metabolic equilibrium. By leveraging our expertise in endoscopic therapies, and our insights into the biology of the gut and pancreas, we believe our therapeutic approaches, if approved, have the ability to alter the paradigm for treating T2D by remediating the most fundamental causes of the disease.

Benefits of Our Approach

Independent scientific observations have demonstrated that a dysfunctional duodenal mucosa contributes to insulin resistance, which over time can potentially lead to T2D. Left unchecked, insulin resistance can shift the body's metabolic set-point and lead to a broader set of other serious diseases, including CVD, PCOS and NAFLD, among others. Building upon established independent evidence that bypassing the duodenum can not only improve insulin resistance, but also improve blood glucose levels, we have developed Revita to achieve a similar physiologic benefit in T2D through a scalable, minimally invasive, outpatient procedure.

Our technology leverages these observations and the additional insights we have gained through our clinical studies thus far regarding the role of the lining of the duodenum in insulin resistance and the impact of ablation on potentially correcting the structure and function of the duodenal lining. Revita is designed to disrupt nutrient absorption and address the abnormal neurohormonal signals in the duodenum by targeting and ablating the diseased mucosa in patients with T2D.

We believe that treating the lining of the duodenum with our ablation technology has the potential to change the way patients with metabolic diseases are treated. Revita has been granted Breakthrough Device designation to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin. We intend to study the broad potential of Revita across various subpopulations of T2D, eventually moving to the prediabetes population with the goal of stopping the progression of disease in high-risk individuals.

We believe that Revita's unique individual features combine to provide a significantly differentiated solution to T2D, offering the following potential benefits:

- ***Real World Outcomes.*** Revita does not rely on perfect patient adherence or persistence to chronic therapy for its anticipated clinical effects because it is a procedural therapy, unlike diet and lifestyle interventions or pharmacologic management. As a result, the benefits of the Revita DMR Procedure are intended to be conferred at the time of the procedure and not reliant upon ongoing therapeutic maintenance. This allows a shift in patient focus from escalating chronic disease management burden to ongoing health maintenance after the procedure.

- ***Broad Implementation.*** Revita leverages familiar skillsets of advanced endoscopists, can potentially be incorporated into the endoscopist workflow, is intended to fit into most endoscopy suites, typically requires less than five cases for the endoscopist to acquire proficiency, and is designed to be an outpatient procedure that can be performed by a trained therapeutic endoscopist in less than an hour. In addition, in clinical studies to date, over 95% of endoscopic procedures have successfully ablated the target treatment area. Today, over 20,000,000 endoscopies are performed each year in the United States, including over 600,000 advanced endoscopic procedures, by nearly 10,000 gastroenterologists. The Revita DMR Procedure is designed to be a simple add-on procedure to the 4.7 million endoscopies performed on T2D patients annually.

- ***Patient Friendly.*** Revita is designed offer a straight-forward, outpatient, endoscopic procedural experience for patients, requiring less than a half-day visit, and allowing patients to typically return to their normal daily lives and work the very next day. Furthermore, the Revita DMR Procedure has thus far been observed to be compatible with other current interventions for T2D in broad use, including diet and lifestyle, and existing and upcoming pharmacologic therapies.

- ***Significant Health Savings.*** Patients on insulin cost approximately $10,000 more to payors annually than patients on oral therapy. Therefore, with approximately seven million T2D patients in the United States currently on insulin therapy, of whom five million potentially meet the requirements for the Revita DMR Procedure, the incremental payor addressable healthcare burden for patients on insulin therapy in the United States is approximately $50 billion annually. Revita, in combination with at least one ongoing OAD and lifestyle counseling, has been observed to have a statistically significant mean HbA1c reduction of 1.0% (n=27) and a statistically significant mean FPG reduction of 32 mg/dL (n=28) at 24 months in a long-term follow-up study of the PP population in our Revita-1 feasibility study. In addition, Revita, in combination with a glucagon-like peptide-1 receptor agonist and lifestyle counseling, has been observed to help eliminate the need for insulin in eight of 15 patients (statistically significant as compared to baseline) at 18 months in a long-term follow-up study of the PP population in our INSPIRE pilot study. Based on these observations, we believe Revita may help enhance disease control and thereby reduce pharmacological expenditure and improve health outcomes for patients and health systems.

- ***Disease Modification.*** Revita is designed to target and reduce the neurohormonal signal leading to insulin resistance, the underlying metabolic defect of T2D and other metabolic diseases. This modification of underlying disease progression can potentially improve the health of the pancreas, liver, and other end organs associated with metabolic diseases. As a consequence of this benefit, Revita is designed to offer an outpatient, endoscopic procedural therapy alternative to daily injectables and chronic glucose monitoring, thereby potentially offering greater ease and convenience for patients with T2D and their caregivers.

- ***Tolerability.*** In clinical studies to date, Revita has been observed to be generally well tolerated, with most patients resuming normal daily activities one day after the procedure and none requiring prescription pain medications. We believe our proprietary SureLift technology enables isolation of the mucosa from deeper tissue structures, sparing pain fibers in the muscle and reducing risk of injury. Long-term follow-up has shown no evidence of late-adverse events, pancreatitis, infection, or malabsorption. Post-procedure biopsy and imaging studies have shown full healing of the intestinal mucosa without ongoing fibrosis or scarring.

- ***Mechanism, Durability, Repeatability.*** Revita is designed to improve metabolic health, blood glucose levels, and weight in patients with inadequately controlled T2D. Based on a long-term follow-up study of the PP population in our Revita-1 study, we observed that Revita, in combination with at least one ongoing OAD and lifestyle counseling, had a statistically significant mean HbA1c reduction of 1.0% (n=27) and a statistically significant raw change in weight of -3.1 kg (n=25) in patients at 24 months. In addition, we believe that SureLift can enable repeat Revita procedures over time. After the commercial launch of Revita, if approved, we may conduct a PAS to evaluate the safety and effectiveness of potential repeat procedures, should they be necessary.

- ***Modular System.*** The Revita console is designed to support the DMR procedure and can also potentially be used to support our Rejuva gene therapy platform, which provides precise local delivery of gene therapy to the pancreas, in a single endoscopic procedure performed in a single setting.

Revita Overview

Device Overview

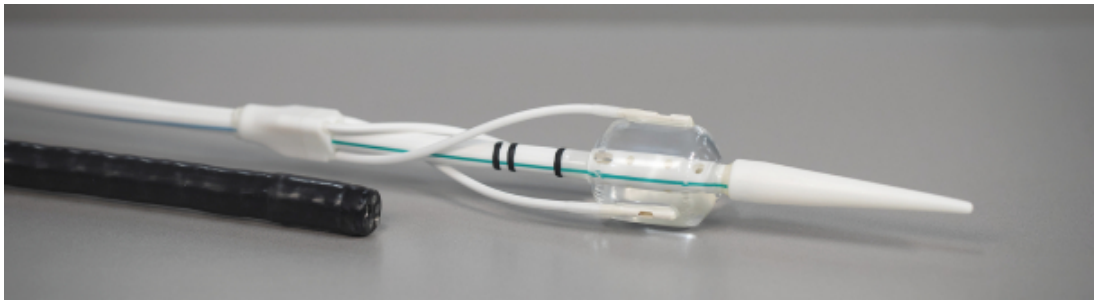
Revita is comprised of (i) the Revita console that houses our proprietary technology and software, and (ii) a single-use Revita DMR catheter and single-use lineset. The console's touchscreen-based graphical user interface is designed to provide ease-of-use and clear guidance on the performance and progress of the procedure

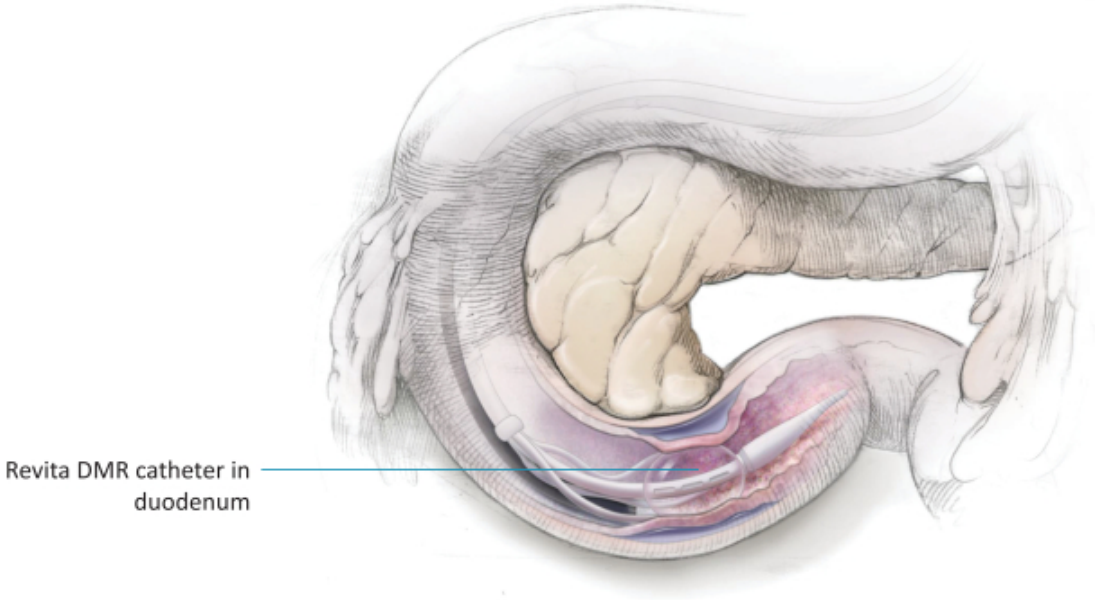
for the physician. The console is designed to control the temperature of the ablative and cooling fluid, vacuum suction, facilitate the delivery of saline for the submucosal lift and the pressure and flow rate of water during the ablation cycle. In addition, the console houses sensors that are designed to monitor temperature, pressure and procedure status. We believe the console enables a targeted ablation process by enabling our proprietary SureLift safety mechanism and reducing penetration of heat to deeper tissues during the hydrothermal ablation procedure, and potentially reduces the risk of physician error by automating certain steps of the treatment process by guiding the physician step-by-step through the procedure. The image below depicts a prototype rendering of the modular Revita console with the current touchscreen user interface. The catheter and graphical user interface are currently being used in our Revitalize-1 clinical study but the Revita console hardware below is not. We plan to seek approval from the FDA of a supplemental PMA for this console design modification.

Modular Revita Console Powered by an Intuitive Touchscreen User Interface

The Revita DMR catheter is comprised of three outward-facing ports on the exterior of our novel ablation balloon with a control handle on the proximal end. Each port on the catheter has an opening whose size and shape is designed to enable suction to selectively pull mucosal and submucosal tissue into the port, while preventing the deeper muscularis tissue from being pulled in. In addition, the catheter is thin, flexible and narrow, and is designed to be deliverable and trackable across the stomach into the small intestine over a standard endoscopic guidewire. The image below depicts the Revita DMR catheter.

Revita DMR Catheter





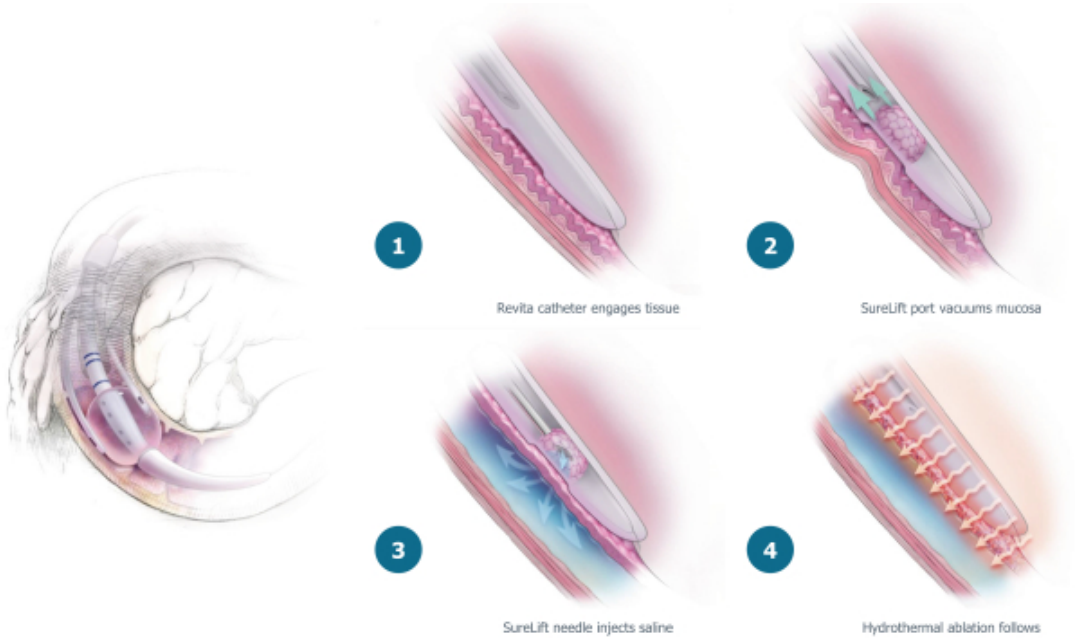
Procedure Overview

The Revita DMR Procedure is designed to be a minimally invasive, outpatient, endoscopic procedural therapy using a proprietary balloon catheter that is uniquely designed for the duodenal mucosa in a procedure that typically lasts less than an hour. Revita is designed to target the mucosal surface for ablation and induce intestinal stem cell-mediated regeneration. The procedure is performed by a trained endoscopist while the patient is under conscious sedation or general anesthesia. With the help of the Revita console, certain steps of the procedure are designed to be highly automated, which we believe minimizes the risk of physician error.

The procedure involves inserting the distal end of the single-use Revita catheter through the mouth over a guidewire past the stomach and into the duodenum, using fluoroscopy to assist placement. The catheter is then positioned distal to the ampulla of Vater (i.e., the hepatopancreatic duct where bile salts and pancreatic enzymes enter the GI tract) under direct endoscopic visualization. The procedure then involves a repeated sequence of mucosal lifting (i.e., SureLift) and hydrothermal ablation steps.

SureLift. Our proprietary SureLift procedural step involves an automated, circumferential instillation of saline into the submucosal space of the duodenum. This step is initiated through the user interface of the console and enables the lifting of the mucosa away from the underlying muscle layer. The catheter balloon is expanded with fluid to allow the catheter to engage with the mucosa and a vacuum connected to the console draws the mucosa into each of three injection ports on the catheter. The user interface of the console is then used to initiate saline delivery to the submucosal space via needles within the vacuum ports. SureLift is designed to create a thermal barrier between the mucosa and the underlying muscular layer in order reduce the risk of discomfort or unintended thermal injury, and to enable repeated procedures by ensuring that the mucosa can be safely lifted before performing thermal ablation.

SureLift Designed to Create a Protective Thermal Barrier for a Well Tolerated Procedure



Hydrothermal Ablation. After SureLift is completed in a region of the duodenum, hydrothermal ablation is initiated through the console user interface. The ablation cycle involves the introduction and recirculation of water within the balloon. We believe this sequence of steps provides a controlled, uniform, "thin layer" ablation of the mucosa and superficial submucosa and potentially further reduces the risk of injuring deeper tissues. The first step fills the balloon with cold water to cool the duodenal tissue below body temperature prior to ablation. The second step is intended to deliver a precise dose of hydrothermal energy to the tissue to create a controlled coagulative ablation. The third step is intended to remove any residual heat from the tissue and to prevent unintended conduction of heat within the tissue.

The SureLift and hydrothermal ablation steps are continued sequentially along the length of the duodenum, extending from just beyond the ampulla of Vater and proceeding distally until the full length of the duodenum is treated. The sequential SureLift and hydrothermal ablation steps are designed to ensure the spatial and temporal alignment of the ablation within the previously lifted region before the thermal protective saline barrier dissipates. We have designed Revita's hydrothermal ablation to be coagulating, where the proteins in the tissue are denatured but the tissue remains in place. In addition, our ablation procedure is designed to prevent bleeding and to allow overlapping ablations without excessive depth of ablation.

Upon completion of the procedure, the guidewire, catheter and endoscope are removed, leaving no long-term implant in the GI tract. The patient is typically discharged on the same day and is prescribed a graduated post-procedure diet, starting with liquids and progressing to pureed foods and soft foods. Similar to other routine upper-GI endoscopic procedures, if Revita is approved, we anticipate that patients will resume normal activities the day after their procedure, which is supported by our observations to date.

Clinical Data Overview: Revita

We have evaluated the Revita DMR Procedure in nearly 300 patients in multiple clinical studies across numerous sites in South America, Europe and the United States. To date, we have observed that the Revita DMR

Procedure, in combination with certain ADAs and lifestyle counseling, was found the be generally well tolerated and improved glycemic control. We are also currently evaluating the Revita DMR Procedure in our Revitalize-1 pivotal clinical study in patients with inadequately controlled T2D despite being on metformin, up to two additional ADAs, and long-acting insulin. Based on the data observed in our previously conducted clinical studies, we believe that the Revita DMR Procedure has the potential to procedurally treat the organ-level root cause of metabolic diseases, such as T2D.

The table below summarizes our ongoing, planned and completed clinical studies for the Revita DMR Procedure.

Study and Status	Study Design	Primary Objectives	Milestones / Results
Revitalize-1. Pivotal clinical study in patients with inadequately controlled T2D despite being on metformin, up to two additional ADAs, and long-acting insulin Commenced in March 2021	• Stage 1: open-label, single-arm training stage • Stage 2: Randomized, double-blind, crossover, sham-controlled, multi-center • ~15 cm DMR • Two arms: DMR and sham • Stage 1: up to 140 patients • Stage 2: up to 420 patients	• Stage two: evaluate, among other things, the effects of the Revita DMR Procedure on reducing HbA1c to less than or equal to 7% at 24 weeks without the need for insulin	• Open-label data expected in late 2022 • Topline data expected in 2024
Revitalize-2. Pivotal clinical study in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy Planned	• Stage 1: open-label, single-arm training stage • Stage 2: Randomized, double-blind, sham-controlled, multi-center • Two arms: DMR and sham • Stage 1: up to 110 patients • Stage 2: up to 400 patients	• Evaluate the efficacy of the Revita DMR Procedure on glycemic improvement without the need for insulin at 24 weeks and avoidance of escalation to insulin at 48 weeks	• Initiate study in second half of 2022

Study and Status	Study Design	Primary Objectives	Milestones / Results
Revitalize-3. Proof-of-concept pilot study in patients with high risk of prediabetes Planned	• Open-label (*in silico* real world control) • ~15 cm DMR • Single arm • Up to 300 patients	• Evaluate the effectiveness of the Revita DMR Procedure on reducing the risk of developing T2D	• We expect to submit an IDE and comparable documents for this study to the FDA and comparable foreign regulatory authorities or notified bodies in 2022
U.S. Pilot. Pilot study in patients with sub-optimally controlled T2D despite being on metformin in combination with one to two additional OADs Completed (prematurely ended)	• Randomized (2:1), double-blind, crossover, sham-controlled, multi-center • Two arms: DMR and sham • 9 patients • ~10 cm DMR • No formal statistical powering	• Evaluate the safety and efficacy of the Revita DMR Procedure on certain glycemic endpoints	• The Revita DMR Procedure was generally well tolerated • As agreed with the FDA, the study was prematurely ended due to the COVID-19 pandemic and subsequent authorization to proceed with the Revitalize-1 study
Revita-2. Clinical study in patients with sub-optimally controlled T2D despite being on an OAD and/or metformin Completed	• Randomized, double-blind, crossover, sham-controlled, multi-center • ~10 cm DMR • Two arms: DMR and sham • 108 patients	• Evaluate the safety and efficacy of the Revita DMR Procedure on certain T2D-related endpoints	• Baseline reduction of HbA1c, MRI-PDFF, HOMA-IR and weight when compared to the sham arm (p*=<0.05) • The Revita DMR Procedure was generally well tolerated
INSPIRE. Investigator-initiated pilot study in T2D patients on long-acting insulin Completed	• Open-label, single-center • ~15 cm DMR • Single arm • 16 patients	• Evaluate the feasibility of eliminating insulin therapy in T2D patients by combining the Revita DMR Procedure with a GLP-1 and lifestyle counseling	• 69%, 56% and 53% of patients at 24 weeks, 48 weeks and 72 weeks, respectively, were off insulin therapy with an HbA1c of 7.5% or less
Revita-1. Feasibility study in patients with poorly controlled T2D despite at least one OAD Completed	• Open-label, multi-center • ~9 cm DMR • Single arm • 46 patients	• Evaluate the safety and effectiveness of the Revita DMR Procedure on certain glycemic endpoints	• Baseline mean HbA1c reduction of 0.9% at 24 weeks (p*= <0.001) • The Revita DMR Procedure was generally well tolerated

Study and Status	Study Design	Primary Objectives	Milestones / Results
Revita First-in-Human. Clinical study in patients with poorly controlled T2D despite at least one OAD Completed	• Open-label, single-center • Single arm: LS-DMR (~9 cm) and SS-DMR (~3 cm) • 57 patients	• Evaluate the safety and feasibility of the Revita DMR Procedure over variable lengths of the duodenum	• Baseline mean HbA1c reduced by 2.5% at 12 weeks (LS-DMR) (p*=<0.05) • Baseline mean HbA1c reduced by 1.2% at 12 weeks (SS-DMR) (p*=<0.05) • The Revita DMR Procedure was generally well tolerated; duodenal stenosis observed in three patients with good resolution post-balloon dilation

* p-value represents the chance that the observed results occurred by chance alone. A p-value of less than 0.05 is considered statistically significant.

Key Metrics

The outcomes of our clinical studies are evaluated by a number of well-known validated glycemic metrics, including:

Glycosylated Hemoglobin (HbA1c %). HbA1c reflects average levels of blood glucose over the previous two to three months and is the most widely used clinical test to estimate mean blood glucose and monitor glycemic control.

Fasting Plasma Glucose (mg/dL or mmol/L). FPG measures the serum glucose concentration after an overnight fast of at least eight hours providing an instantaneous measure of glucose homeostasis.

Oral Glucose Tolerance Test. A oral glucose tolerance test, or OGTT, evaluates beta cell function after a patient ingests a fixed glucose solution. To perform the test, blood glucose is measured immediately prior to consumption and typically every 30 minutes two hours after consumption. Area under the curve, or AUC, OGTT is the calculation of the total excess of blood glucose measured during the course of the OGTT.

Revitalize T2D Program Insights

Our Revitalize T2D program design has been informed by our prior clinical studies and expertise in the field of metabolic diseases, including T2D. We have evaluated the Revita DMR Procedure in over 15 clinical centers and it has been performed by more than 20 different endoscopists. We have followed most patients beyond 12 months post-procedure to observe the long-term safety of the Revita DMR Procedure, including its effects on glucose homeostasis and, in all, we have observed over 500 patient-years of DMR procedure exposure data using Revita. Based on these experiences, we believe the Revita DMR Procedure has the potential to:

- improve glycemic control and eliminate insulin needs in T2D patients on long-acting insulin;
- prevent initiation of long-acting insulin therapy in T2D patients; and
- reduce the risk of developing diabetes in patients with high risk prediabetes.

We are initially focused on developing Revita to improve glycemic control and eliminate insulin needs in T2D patients on long-acting insulin.

Ongoing Revitalize-1 Pivotal Clinical Study

In March 2021, we commenced Revitalize-1 (formerly known as REVITA-T2Di), a randomized, double-blind, crossover, sham-controlled, multi-center pivotal clinical study in patients with inadequately controlled T2D despite being on metformin, up to two additional ADAs, and long-acting insulin. The study is to take place across approximately 35 sites in the United States and the European Union. This pivotal clinical study is designed as a two-stage study and we plan to enroll up to 140 patients in the first stage, and up to 420 patients in the second stage, with a primary endpoint at six months and one year follow-up. The first stage is an open-label, single-arm study for each site to gain experience with the study protocol and the DMR procedure in two to four patients before moving into the pivotal study (i.e., stage 2) with the other patients. The clinical evaluation committee, or the CEC, will provide oversight on adequate training by the endoscopist and site readiness. Once confirmed by the CEC, the site will be opened to enrollment for the pivotal study.

The first ten patients enrolled in stage 1 of this study underwent a drug washout period that subsequently enrolled patients will not undergo. We plan to continue long-term follow-up of these patients in parallel with the other patients from this study. The table below depicts the Revitalize-1 clinical study design.

Revitalize-1 Pivotal Clinical Study Design (n=420 patients)

Treatment	• DMR or sham • Outpatient, same day procedure • Add SGLT2[1]
Population	• Metformin, up to two additional ADAs, and long-acting insulin, except for SGLT2, sulfonylureas, meglitinides and short or rapid acting insulin • Long-acting insulin (20 to 60 units/day) • HbA1c: 7.5% to 9.5% • FPG: ≥ 180 to < 270 mg/dL • BMI: ≤ 40 kg/m2 • Age: 21 to 70 years old

Endpoints	• Primary – Percentage of patients who achieve a HbA1c of ≤ 7% without the need for insulin at 24 weeks, DMR vs. sham
	• Key Secondary – Percentage of DMR patients who achieve a HbA1c of ≤ 7% without an increase in insulin dose from baseline and/or become insulin free at 24 weeks without an increase in HbA1c from baseline
	  • Percentage of patients who achieve a HbA1c of ≤ 7% with a 50% or more reduction in insulin units necessary (including insulin withdrawal) at 24 weeks as compared to baseline, DMR vs. sham
	  • Percentage of patients who become insulin free at 24 weeks, DMR vs. sham
	  • Percentage total body weight loss as compared to baseline at 24 weeks, DMR vs. sham

(1) Empagliflozin will be added as 10 mg initially on day one post-procedure and increased to 25 mg (or max tolerated dose) by day 15

The primary endpoint of Revitalize-1 is the percentage of patients (DMR vs. sham) who achieve a reduction of HbA1c to less than or equal to 7% without the need for insulin at 24 weeks. The sham patients have the opportunity to crossover to the DMR arm at 48 weeks. A trained evaluator plans to assess all patients in the clinic post-procedure at various specified time intervals, including at four weeks, 12 weeks, 24 weeks and 48 weeks.

Key secondary endpoints include the percentage of patients (DMR vs. sham) who achieve a reduction of HbA1c to less than or equal to 7% (i) without an increase in insulin dose from baseline and/or become insulin free at 24 weeks without an increase in HbA1c from baseline and (ii) with a 50% or more reduction in insulin units necessary (including insulin withdrawal) at 24 weeks; the percentage of patients who become insulin free at 24 weeks; and the percentage total body weight loss at 24 weeks.

We expect open-label data from the first stage of this study in late 2022 and topline data in 2024. In addition, the patients and the clinical investigators will remain blinded through 48 weeks, allowing an additional 24 weeks of follow-up data beyond the primary endpoint.

As part of our PMA, we intend to submit the 24-week primary endpoint data and the follow-up data through 48 weeks. We have discussed this study design with the FDA and we believe, based on correspondence with the FDA, this data may support a PMA for Revita to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin. Our decision to establish a 24-week primary endpoint to support a finding of durable effectiveness is based on FDA regulatory precedent for T2D drug products, including our correspondence with the FDA. In addition, we believe longer term data, including 48-week follow-up, may support future claims of durable effectiveness.

If Revita is approved, longer term follow-up studies beyond 48 weeks will likely be performed as part of a PAS, including potentially studying the safety and effectiveness of repeat procedures, should they be necessary. Based on regulatory precedent, we believe a PAS may be conducted in parallel with the commercial launch of Revita.

Interim Data—Stage 1 Drug Washout (REVITA-T2Di) Cohort

We enrolled ten patients who underwent a drug washout period and underwent a screening endoscopy. One patient was found to have an intercurrent condition and was excluded at the time of endoscopy and was not treated. Nine subjects were therefore treated with Revita. All nine procedures were successfully completed across four treating centers by five different endoscopists, including three endoscopists new to Revita as part of this study. In the nine treated patients, there have been no observed adverse events of special interest, or AESIs, device- or procedure-related serious adverse events, or SAEs. One patient who did not tolerate empagliflozin therapy, withdrew from the study for reasons unrelated to Revita. As of January 10, 2022, all eight treated patients followed through at least four weeks of follow-up remained off insulin and any other ADAs they had previously been prescribed prior to enrollment, except for metformin and empagliflozin.

Planned Revitalize-2 Pivotal Clinical Study

We plan to initiate the Revitalize-2 randomized, double-blind, sham-controlled, multi-center pivotal clinical study in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy. The study is to take place across approximately 35 sites in the United States and 20 sites outside of the United States (with more than 50% of patients in the United States). This study is designed as a two-stage study and we plan to enroll up to 110 patients in the first stage, and up to 400 patients in the second stage, for a total of up to 510 patients.

The first stage is an open-label, single-arm study for each site to gain experience with the study protocol and the DMR procedure in patients before moving into the pivotal study (i.e., stage 2) with the other patients. Sites with previous experience performing the DMR procedure will be required to enroll one patient in stage 1, while sites that are nalve to performing the DMR procedure will be required to enroll two patients in this stage. Prior to entering stage 2, the CEC will review performance of the DMR procedure at each site and may recommend enrollment of additional patients in stage 1 at certain individual sites (maximum of two additional patients) if needed to ensure proficiency of the DMR procedure. The table below depicts the Revitalize-2 pivotal clinical study design.

Revitalize-2 Pivotal Clinical Study Design (n=400 patients)

Treatment	• DMR or sham • Outpatient, same day procedure
Population	• Two to three ADAs, except insulin, meglinitides or sulfonylureas • Ongoing or discontinued GLP-1(1) • HbA1c: 8% to 10% • BMI: ≥ 24 and ≤ 40 kg/m2 • Age: 18 to 70 years old
Endpoints	• Primary – Change from baseline in HbA1c at 24 weeks in DMR patients • Key Secondary – Percentage of DMR patients who achieve a HbA1c of ≤ 7% without insulin rescue therapy at 24 weeks

(1) If use of GLP-1 is ongoing, dosing regimen must be stable for at least 12 weeks prior to visit 1

The primary endpoint will be to evaluate the efficacy of the Revita DMR Procedure on the change from baseline of HbA1c at 24 weeks. In addition, the patients and the clinical investigators will remain blinded through 48 weeks, allowing an additional 24 weeks of follow-up data beyond the primary endpoint.

The key secondary endpoint will be to evaluate the percentage of patients who achieve a HbA1c of less than or equal to 7% without insulin rescue therapy at 24 weeks.

Similar to the Revitalize-1 study and FDA regulatory precedent for T2D drug products, we have established a 24-week primary endpoint for the Revitalize-2 study. Further, we plan to keep patients blinded through 48 weeks to allow blinded and controlled safety and effectiveness assessments at 48 weeks. Based on feedback we obtained from the FDA regarding the primary endpoint of the Revitalize-2 study, we believe the FDA may seek an assessment of effectiveness at 48 weeks to better understand the durability of the Revita DMR Procedure as part of a PMA. We intend to discuss durability assessments at 48 weeks further with the FDA. If the Revitalize-2 study is completed subsequent to a potential Revita PMA approval pursuant to the Revitalize-1 study, we plan to use the data from Revitalize-2 to file for an expanded label as part of a PMA supplement.

Planned Revitalize-3 Proof-of-Concept Pilot Study

We plan to initiate Revitalize-3, an open-label proof-of-concept pilot study with real world *in silico* control in patients with a high risk of prediabetes. We expect to enroll up to 300 patients and to follow patients for two to three years after the procedure.

The primary objective of this study will be to evaluate the effectiveness of the Revita DMR Procedure on reducing the risk of developing T2D in these patients. We plan to initiate a follow-up pivotal study.

We expect to submit an IDE and comparable documents for this study to the FDA and comparable foreign regulatory authorities or notified bodies in 2023.

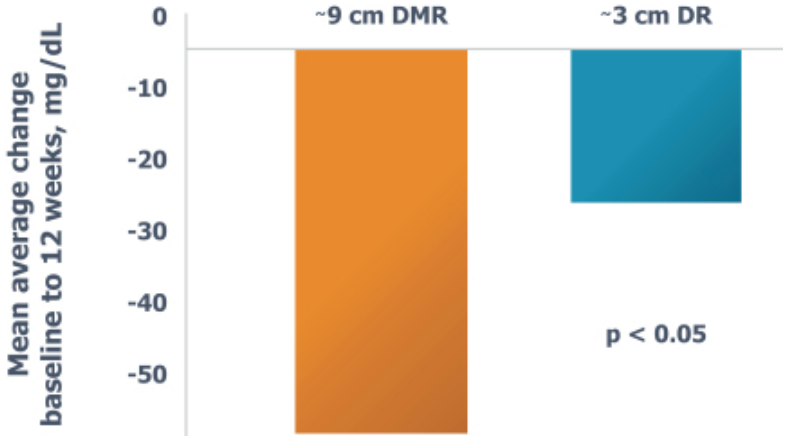
Revita First-in-Human Clinical Study

In 2013, we initiated the Revita first-in-human clinical study in 39 T2D patients. Our inclusion criteria included patients ages 28 to 75, with a baseline HbA1c between 7.5% and 12%, a BMI between 24 and 40, documentation of preserved pancreatic function (as defined by a fasting C-peptide value of greater than or equal to 1 ng/mL), on at least one stable OAD for a minimum of three months and a T2D diagnosis within the past ten years. Patients either received long-segmented ablation (mean length ablated: 9.3 cm), or LS-DMR, or short-

segmented ablation (mean length ablated: 3.4 cm), or SS-DMR. The open-label feasibility study took place in Santiago, Chile and was conducted to evaluate the safety and feasibility of the Revita DMR Procedure over variable lengths of the duodenum. All patients were assessed in the clinic by a trained evaluator post-procedure at various specified time intervals, including at four weeks, 12 weeks and 24 weeks.

This study was designed as a single-arm, open-label feasibility study. The Revita DMR Procedure was observed to be feasible and generally well tolerated, with ablations performed in escalating lengths of the duodenum ranging from 3 cm to 9 cm in length. Exploratory endpoints evaluated included, among others, the baseline mean change of HbA1c and baseline mean change of FPG. We observed that the patients who received LS-DMR had a statistically significant 2.5% reduction in baseline mean HbA1c at 12 weeks post-procedure as compared to 1.2% for the patients who received SS-DMR ($p < 0.05$). At 24 weeks post-procedure, similar baseline mean HbA1c reduction of 1.4% and 0.7% were observed in the LS-DMR and SS-DMR cohorts, respectively, with a statistically significant overall baseline mean HbA1c reduction of 1.2% at 24 weeks in the full cohort (LS-DMR and SS-DMR) ($p < 0.001$). Early and sustained improvement in FPG was also observed among the full cohort, as depicted in the graph below.

Change in FPG in LS-DMR as Compared to SS-DMR at 12 Weeks



The Revita DMR Procedure was observed to be generally well tolerated, with mostly mild and transient GI symptoms. Three patients experienced duodenal stenosis that required an endoscopic balloon dilation with good resolution. We observed no GI bleeds, infection, pancreatitis, or evidence of malabsorption or significant hypoglycemia.

Revita-1 Feasibility Study

In 2015, we initiated an open-label, multi-center feasibility study in 46 patients. Our inclusion criteria included patients ages 28 to 75, with a baseline HbA1c between 7.5% and 11%, a BMI between 24 and 40 kg/m2, on at least one stable OAD for a minimum of three months and had a T2D diagnosis within the past ten years. The study took place across multiple sites in Europe and South America, and was conducted to evaluate the safety and effectiveness of the Revita DMR Procedure on certain glycemic endpoints. Patients either underwent a dual-catheter DMR or single-catheter DMR procedure of nine to ten centimeters and were stratified into the safety population (n=46) or PP population (n=34). All patients were assessed in the clinic by a trained evaluator post-procedure at various specified time intervals, including at four weeks, 12 weeks, 18 weeks and 24 weeks. In addition, we conducted a long-term follow-up study of the PP population through 24 months.

The primary endpoint of the study was to evaluate the baseline mean reduction of HbA1c at 24 weeks. We observed a statistically significant absolute baseline mean HbA1c reduction of 0.9% in the PP population at

24 weeks ($p \leq 0.001$). In addition, we observed a statistically significant baseline mean HbA1c mean reduction of 0.8% and 1.0% in the dual-catheter patients and the single-catheter patients, respectively, in the PP population ($p \leq 0.001$ for both). We also observed a statistically significant absolute baseline mean HbA1c reduction of 1.0% in the PP population at 48 weeks ($p \leq 0.001$).

Secondary endpoints included, among others, baseline mean reduction of FPG, insulin resistance and weight. We also conducted post-hoc analyses of the baseline mean reduction of ALT and AST at 24 weeks. To quantify the reduction in insulin resistance, we used the Homeostatic Model Assessment of Insulin Resistance, or HOMA-IR. This model is able to quantify insulin resistance by evaluating a patients FPG and insulin levels. The table below depicts our observations of these secondary endpoints, including the ALT and AST post-hoc evaluations, at 24 and 48 weeks.

Measurement	Baseline	24 Weeks	24 Week Difference	P-Value*	48 Weeks	48 Week Difference	P-Value*
FPG (mmol/L)	10.7 ± 0.4	9.0 ± 0.4	-1.7 ± 0.5	≤ 0.001	8.9 ± 0.4	-1.8 ± 0.5	≤ 0.001
HOMA-IR	8.2 ± 1.0	5.2 ± 0.8	-2.9 ± 1.1	0.007	4.9 ± 0.6	-3.3 ± 0.9	≤ 0.001
Weight (kg)	90 ± 2	88 ± 2	-2 ± 1	≤ 0.001	88 ± 2	-2 ± 1	≤ 0.001
ALT (IU/L)	40 ± 2	31 ± 1	-8 ± 3	0.016	30 ± 1	-9 ± 3	≤ 0.001
AST (IU/L)	28 ± 2	23 ± 1	-5 ± 2	0.002	22 ± 1	-6 ± 1	≤ 0.001

* P-values resulting from ANOVA repeated measurement analysis with Bonferroni correction

In the long-term follow-up study of the PP population, we observed statistically significant mean changes of HbA1c, FPG and weight. Out of the 34 patients in the PP population, seven patients discontinued follow-up in the HbA1c analysis and six patients discontinued follow-up in the FPG and weight loss analysis prior to the 24-month check-in. The table below depicts our observations in the long-term follow-up study of the PP population at 24 months.

Measurement	Baseline	24 Months	P-Value*
HbA1c	8.5 ± 0.7	7.5 ± 1.1 (n=27)	0.034
FPG (mg/dL)	198.4 ± 41.2	165.9 ± 0.9 (n=28)	< 0.001
Weight** (kg)	88.9 ± 11.8	-3.1 ± 6.0 (n=25)	0.010

* P-values resulting from ANOVA repeated measurement analysis with Bonferroni correction
** Raw change

No unanticipated adverse device effects, or UADEs, or device-related SAEs were reported. Three device-related events occurred in one subject, including two reports of abdominal pain and one report of nausea on the first day after the procedure. Each device-related event was resolved with medication. There were a total of ten SAEs reported in seven patients, one of which was considered procedure-related. The single procedure-related SAE occurred in a single-catheter patient where the patient experienced a mildly elevated body temperature and an increase in C-reactive protein. The investigator elected to keep the patient in the hospital overnight for observation, which made the event an SAE. This event was determined to be not device-related.

The other SAEs reported were patient specific and determined to not be device-related. For example, one patient experienced SAEs from a new diagnosis of lung cancer and died approximately 11 months post-procedure. Overall, the Revita DMR Procedure was observed to be generally well tolerated in the full cohort.

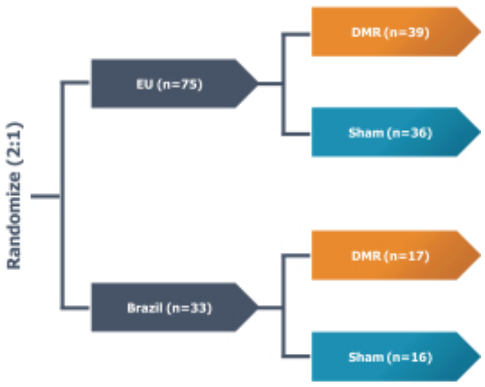
Revita-2 Clinical Study

In March 2017, we initiated a randomized, double-blind, crossover, sham-controlled clinical study in 108 patients with sub-optimally controlled T2D despite being on OADs and/or metformin across multiple sites in Europe and Brazil. The study was conducted to evaluate the safety and efficacy of the Revita DMR Procedure, as measured by certain T2D-related endpoints. The primary endpoints of the study were to evaluate the baseline change of HbA1c and proton density fat fraction (a validated biomarker used to quantify liver fat) through magnetic resonance imaging, or MRI-PDFF, at 24 weeks. Secondary endpoints included, among others, (i) the absolute baseline change of MRI-PDFF in patients with a baseline MRI-PDFF of greater than 5%, indicating NAFLD or NASH, (ii) the absolute change of MRI-PDFF in patients with a baseline FPG of 180 mg/dL or greater, (iii) reduction in insulin resistance and (iv) weight loss.

All patients initially went through a 4-week run-in period to confirm lack of blood glucose control in conjunction with medication compliance and nutritional counseling. Patients then either underwent the DMR procedure or the sham procedure. The dosage of each patient's OADs was held constant from the start of the run-in period through week 24. All patients were assessed in the clinic by a trained evaluator post-procedure at various specified time intervals, including at four weeks, 12 weeks, 18 weeks and 24 weeks. The table below depicts the Revita-2 clinical study design.

Revita-2 Clinical Study Design (n=108 patients)

Treatment	• DMR or sham • Outpatient, same day procedure
Population	• OADs and/or metformin[1] • HbA1c: 7.5% to 10% • Fasting insulin >7.0 µU • BMI: ≥ 24 and ≤ 40 kg/m2 • Age: 28 to 75 years old
Endpoints	• Primary – Baseline change of HBA1c and MRI-PDFF at 24 weeks
	• Secondary – Baseline change of MRI-PDFF in patients with baseline ≥ 5% MRI-PDFF and baseline FPG > 180 mg/dL • Reduction of HOMA-IR • Weight loss



(1) No changes in medications in 12 weeks prior to study entry

In the overall study, we observed an HbA1c reduction of 1.0% in DMR group as compared to 0.7% in sham group, and an MRI-PDFF reduction of 5.4% in DMR group as compared to 2.9% in sham group. A pre-specified test of heterogeneity in the statistical analysis plan led to the separation of the analyses of the Brazilian and European intention-to-treat populations. This separation was due to (i) the lack of homogeneity between the populations identified by our statistical analysis plan, (ii) key clinical observations demonstrating the Brazilian population had implausible large improvements in glucose control and weight, including patients in the sham arm, which was inconsistent with results observed in the European sham patients, (iii) independent on-site audits in Brazil showed key differences compared to Europe in the documentation of use of medications (changes in medications) and more intensive glucose monitoring and nutritional guidance, and (iv) other post-hoc statistical analyses confirming key differences in the two populations.

Both HbA1c and MRI-PDFF primary endpoints were met in the European population and demonstrated statistically significant superiority of DMR as compared to sham.

European Population Results

We observed a 0.60% baseline mean reduction of HbA1c at 24 weeks in the European DMR arm, which was statistically significantly greater than the 0.30% reduction observed in the European sham arm (p=0.033). At 24 weeks post-procedure, we observed a 5.40% absolute baseline median reduction of MRI-PDFF in the European DMR arm, which was statistically significantly greater than the 2.36% reduction observed in the European sham arm (p=0.039).

Secondary endpoints included, among others, (i) the absolute baseline change of MRI-PDFF in patients with a baseline MRI-PDFF of greater than 5%, indicating NAFLD or NASH, (ii) the absolute change of MRI-PDFF in patients with a baseline FPG of 180 mg/dL or greater, (iii) reduction in insulin resistance and (iv) weight loss. We observed a 5.4% absolute baseline median reduction of MRI-PDFF in the European DMR arm at 12 weeks for these patients, which was statistically significantly greater than the 2.4% reduction observed in the European sham arm (p=0.025). We also observed a statistically significant difference in the absolute change of MRI-PDFF in patients with a baseline FPG of 180 mg/dL or greater in the European DMR arm (-8.0%) as compared to the European sham arm (-2.1%; p=0.006).

We observed a 1.32 median reduction of HOMA-IR in the European DMR arm at 24 weeks, which was significantly greater than the 0.43 reduction observed in the European sham arm (p=0.060). In addition, we observed a statistically significant median weight loss of 2.35 kg in the European DMR arm as compared to a median weight loss of 1.35 kg in the European sham arm (p=0.012).

Brazilian Population Results

The results we observed in the Brazilian population were similar to those seen in the European population, except for the MRI-PDFF endpoint. We observed a greater reduction of HbA1c, HOMA-IR and weight in the Brazilian DMR arm as compared to the Brazilian sham arm at 24 weeks. These results were not statistically significant due to the small sample size of the Brazilian population and the separation of these populations as discussed above. Because of the small sample size of the Brazilian population and the findings of the audit, these results should be interpreted with caution.

Adverse Events

No UADEs or device-related SAEs were reported. AESI rates were comparable between the DMR and sham arms. In the Brazilian population, 11.8% of the randomized DMR patients experienced SAEs, all of which were considered to be related to the study procedure and not Revita. In addition, there were no clinical or laboratory signs of adverse events related to malabsorption, anemia, pancreatitis, biliary complications, or infection reported. The table below depicts the AEs observed in the study, separated by European and Brazilian sites, as part of the analyses described above.

	Europe						Brazil					
	DMR n=39			Sham n=37			DMR n=17			Sham n=16		
	# of events	n (%)	95% CI	# of events	n (%)	95% CI	# of events	n (%)	95% CI	# of events	n (%)	95% CI
Summary (through 24 weeks post-treatment)												
SAE	0	0	(0.0 to 9.0)	0	0	(0.0 to 9.5)	3	2 (11.8)	(1.5 to 36.4)	0	0	(0.0 to 20.6)
UADE	0	0	(0.0 to 9.0)	0	0	(0.0 to 9.5)	0	0	(0.0 to 19.5)	0	0	(0.0 to 20.6)
AESI	19	13 (33.3)	(19.1 to 50.2)	16	10 (27.0)	(13.8 to 44.1)	74	12 (70.6)	(44.0 to 89.7)	76	10 (62.5)	(35.4 to 84.8)
Most common (≥5%) AESIS by preferred term (≤30 days pot-treatment)												
Abdominal pain	9	7 (17.9)	(7.5 to 33.5)	2	2 (5.4)	(0.7 to 18.2)	6	5 (29.4)	(10.3 to 56.0)	2	2 (12.5)	(1.6 to 38.4)
Diarrhea	1	1 (2.6)	(0.1 to 13.5)	2	2 (5.4)	(0.7 to 18.2)	1	1 (5.9)	(0.2 to 28.7)	1	1 (6.3)	(0.2 to 30.2)
Nausea	1	1 (2.6)	(0.1 to 13.5)	0	0	(0.0 to 9.5)	2	2 (11.8)	(1.5 to 36.4)	0	0	(0.0 to 20.6)
Vomiting	1	1 (2.6)	(0.1 to 13.5)	0	0	(0.0 to 9.5)	1	1 (1.59)	(0.2 to 28.7)	0	0	(0.0 to 20.6)
Hypoglycemia	3	3 (7.7)	(1.62 to 20.9)	3	2 (5.4)	(0.7 to 18.2)	11	6 (35.3)	(14.2 to 61.7)	21	7 (43.8)	(19.8 to 70.1)
Most common (≥5%) AESIS by preferred term (>30 days pot-treatment)												
Abdominal pain	1	1 (2.6)	(0.1 to 13.5)	2	2 (5.4)	(0.7 to 18.2)	0	0	(0.0 to 19.5)	0	0	(0.0 to 20.6)
Hypoglycemia	1	1 (2.6)	(0.1 to 13.5)	4	2 (5.4)	(0.7 to 18.2)	53	5 (29.4)	(10.3 to 56.0)	52	8 (50.0)	(24.7 to 75.4)

INSPIRE Pilot Study

In 2017, van Baar et al. initiated an open-label, single-center pilot study in 16 patients with T2D on guideline-directed long-acting insulin. The study took place in the Netherlands and was conducted to evaluate the feasibility of eliminating insulin therapy in T2D patients by combining the Revita DMR Procedure with a GLP-1 and lifestyle counseling, including a tailored diet. All patients were assessed in the clinic by a trained evaluator post-procedure at various specified time intervals, including at 6 months, 12 months and 18 months, and the results of this study were published in *Gastrointestinal Endoscopy*. The table below depicts the INSPIRE pilot study design.

INSPIRE Pilot Study Design (n=16)[2]

Treatment	• DMR or sham • Outpatient, same day procedure • Add GLP-1[1]
Population	• Long-acting insulin[2] • HbA1c: ≤ 8% • C-reactive peptide ≥ 0.5 ng/mL • BMI: ≥ 28 and ≤ 40 kg/m2 • Age: 25 to 75 years old
Endpoints	• Primary – Percentage of patients free of insulin therapy through 6 months with HbA1c ≤ 7.5% at 6 months • Secondary – Baseline reduction of HbA1c, HOMA-IR and weight at 6 months

(1) Liraglutide, a GLP-1, was introduced two weeks post-procedure with a stepwise dose increase to 1.8 mg/day or max tolerated dose
(2) Insulin therapy discontinued immediately after DMR procedure

The primary endpoint of the pilot study was the percentage of patients free of insulin therapy through 6 months with an HbA1c less than or equal to 7.5% at 6 months. Investigators observed 69% of patients were

free of insulin therapy with an HbA1c less than or equal to 7.5% at 6 months. This result was not statistically significant.

Secondary endpoints were the changes in multiple glycemic and metabolic parameters and the percentage of patients free of insulin with an HbA1c less than or equal to 7.5% at 12 and 18 months, respectively. Out of the 16 patients, one discontinued follow-up prior to the 18-month check-in. The table below depicts the secondary endpoint observations.

Measurement	Baseline	12 Months	P-Value	18 Months	P-Value
	Glycemic parameters				
Patients off insulin	0 (0)	9 (56)		8 (53)*	0.0008
HbA1c	7.5 (7.1-7.9)	7.3 (6.6-8.2)	0.690	7.1 (6.6-7.5)	0.208
HOMA-IR	8.4 (4.3-12.0)	3.8 (2.4-7.9)	0.015	3.9 (2.0-6.0)	0.006
FPG (mmol/L)	10.1 (8.9-12.0)	7.1 (6.6-9.5)	0.006	7.3 (6.7-8.4)	0.011
Fasting insulin (pmoll/L)	104 (49-178)	71 (45-121)	0.116	63 (34-110)	0.036
Fasting C-peptide (nmol/L)	0.63 (0.55-0.91)	0.58 (0.39-0.70)	0.224	0.46 (0.39-0.59)	0.245
	Metabolic parameters				
Weight (kg)	87.8 (80.2-99.7)	80.8 (73.2-95.8)	0.001	80.7 (73.8-96.8)	0.001
BMI (kg/m2)	28.8 (26.5-31.7)	27.7 (23.4-30.1)	0.001	26.4 (23.5-30.2)	0.001
MRI-PDFF**	8.1 (4.0-13.5)	5.6 (2.8-10.9)	0.035		

* One patient did not agree to continue follow-up to 18 months
** MRI-PDFF was known in 15 of 16 patients

We believe this study demonstrated that a single Revita DMR Procedure in combination with GLP-1 and lifestyle counseling, may eliminate the need for insulin therapy in T2D patients while improving glycemic control and overall metabolic health.

U.S. Pilot Study

In March 2019, we initiated a randomized, double-blind, crossover, sham-controlled pilot study. Our inclusion criteria included patients ages 28 to 65, with a baseline HbA1c between 7.5% and 9.5%, a BMI between 28 and 40 kg/m2 and were on metformin in combination with one to two additional OADs across multiple sites in the United States. The doses of two of the OADs must have been at least half the maximum labeled dose (or highest tolerated) with no changes in medication in the 12 weeks prior to screening. The plan was to randomize 18 patients in a 2:1 ratio in favor of DMR. However, as discussed and agreed with FDA, the study was prematurely ended in July 2020 due to the COVID-19 pandemic and subsequent approval of the Revitalize-1 trial.

In total, nine patients were enrolled in this study and one patient randomized to the DMR arm received the sham procedure, which was considered a major protocol violation. The primary objective of the study was to evaluate the feasibility and safety of the Revita DMR Procedure. As a pilot evaluation, no statistical or powering assumptions were developed and implemented regarding the efficacy evaluation. Unblinding occurred at week 24 and sham treatment arm subjects who accepted the offer to crossover received DMR treatment and were followed for an additional 24 weeks.

All patients initially went through a 4-week run-in period to assess the stability of glycemic control in conjunction with medication compliance and diet and exercise counseling. Patients then either underwent the DMR procedure or the sham procedure. The dosage of each patients OADs was held constant from the start of the run-in period through week 24. All patients were assessed in the clinic by a trained evaluator post-procedure at various specified time intervals, including at four weeks, 12 weeks, 18 weeks, and 24 weeks.

The primary endpoint of the study was to evaluate the change in baseline HbA1c at 24 weeks as compared to sham using descriptive statistics. Baseline was defined as the last observation recorded prior to the DMR or sham procedure. We observed endpoint data in only three patients because of the onset of the COVID-19 pandemic. In those three patients, a 0.33% baseline mean reduction of HbA1c at 24 weeks in the DMR arm was observed as compared to a 0.70% baseline mean reduction of HbA1c at 24 weeks in the sham arm. In addition, we observed a 0.80% baseline mean reduction of HbA1c at 18 weeks in the three crossover patients.

Due to the small sample size of this study, we were not able to draw any firm conclusions from the data presented above.

No SAEs, UADEs or severe treatment-emergent adverse events, or TEAEs, were reported. Incidents of AESIs, such as hypoglycemia and GI-related complications, were similar between the DMR and sham arms. Device-related TEAEs were reported at a lower incidence in the DMR arm, including the crossover patient, as compared to the sham arm. Each of the device-related TEAEs in the DMR arm, including diarrhea, oropharyngeal pain, abdominal distension, nausea and pyrexia, were also reported in the sham arm, except for nausea and fever.

Preclinical Studies Overview: Revita

We have evaluated the duodenum's role in glucose homeostasis in multiple preclinical studies, including a proof-of-concept study and large animal, human-excised tissue and human cadaveric studies. Taken together, we believe these studies provided support for the feasibility and safety of the Revita DMR Procedure before proceeding to human clinical studies.

Preclinical Studies: Proof-of-Concept

We conducted a preclinical study in a Goto-Kakizaki, or GK, rat model of T2D to evaluate whether selective removal of the duodenal mucosa may improve glucose homeostasis. The GK rat model was selected because it has been validated in bariatric surgical procedures to replicate human post-surgical improvement in glucose parameters. Due to the limitations of rat anatomy, the study was performed using abrasion rather than ablation. With a new catheter abrasion tool, rats were sedated, instrumented and had the first ten centimeters of their intestinal mucosa abraded. We observed that the abrasion of the intestinal mucosa resulted in a 34% improvement in AUC-OGTT blood glucose control (n=9) compared to sham-operated rats (n=5).

Preclinical Studies: Feasibility and Safety

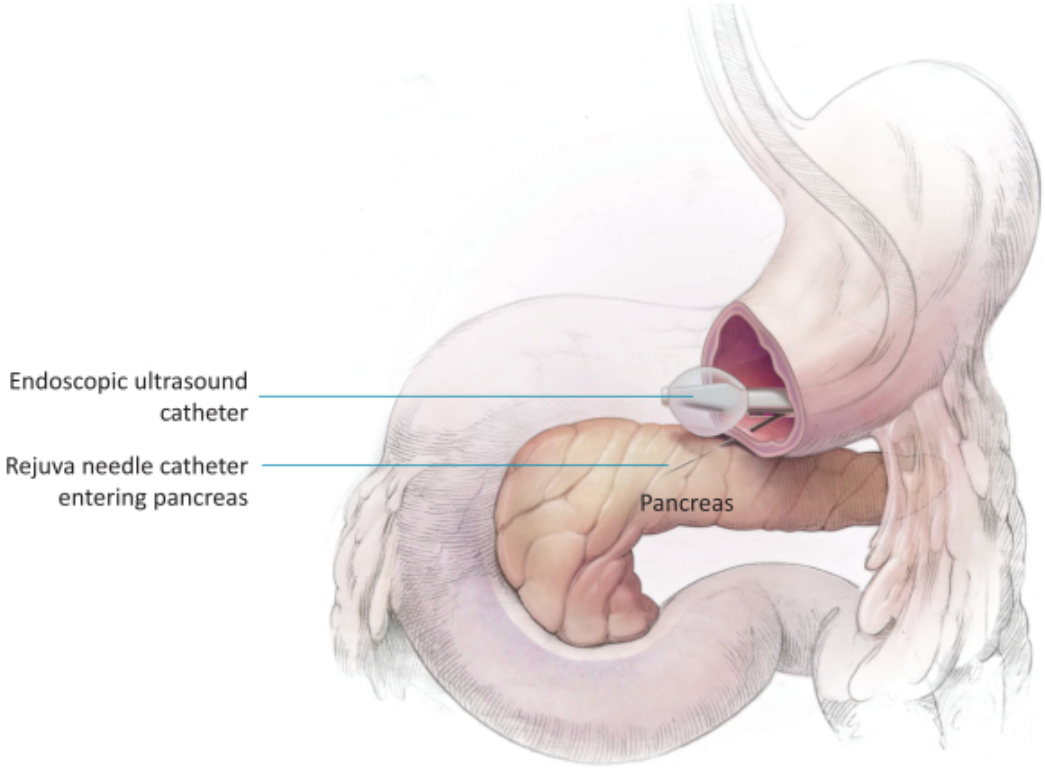
We conducted preclinical studies in large animals, human-excised duodenal tissue and human cadavers to evaluate whether the Revita DMR Procedure may be feasible and tolerated in humans. Large animal studies were performed in Yorkshire pigs to assess the tolerability, feasibility and timeline of tissue healing following the DMR procedure. Human-excised duodenal tissue studies were performed to assess the feasibility of the Revita DMR Procedure in patients, which requires independent verification because of the anatomical differences in the duodenum between humans and animals. Lastly, human cadaveric studies were performed to interrogate catheter delivery and procedure development.

Preclinical Development Overview: Rejuva Gene Therapy Platform

Under our novel Rejuva gene therapy platform, we are focused on developing a disease-modifying gene therapy to address the beta cell dysfunction in T2D patients. Our Rejuva gene therapy candidate is designed to be

administered through an endoscopic procedure directly into the pancreas. The gene therapy candidate is designed to utilize an AAV serotype carrying a GLP-1 receptor analogue transgene to express this targeted protein in pancreatic beta cells. We plan to evaluate its effects on insulin production and glucose homeostasis in multiple preclinical studies. We are additionally evaluating the potential to deliver the gene therapy candidate to the pancreas through a proprietary endoscopic ultrasound enabled needle catheter and direct intraparenchymal injection in porcine feasibility and safety preclinical studies.

Rejuva Needle Catheter Delivers Genetic Medicine via Direct Intraparenchymal Administration



Preclinical Studies: Proof-of-Concept and Planned Studies

In a proof-of-concept preclinical study in a diabetic mouse model, we observed a statistically significant average reduction of fasting blood glucose levels of 54% ($p < 0.0001$) and a statistically significant increase in insulin production of 38% ($p < 0.01$) during a glucose tolerance test at a 5-week time point after a single administration of a certain Rejuva gene therapy candidate compared to the control vector.

We plan to continue *in vitro* and *in vivo* studies evaluating potential device and gene therapy candidate optimization parameters and route of administration in preclinical safety and efficacy studies on a path toward our first gene therapy candidate nomination in 2023.

Commercialization Strategy

We intend to submit a PMA for Revita after we complete the Revitalize-1 study, including the follow-up study through 48 weeks. If approved, longer term follow-up studies beyond 48 weeks will likely be performed as

part of a PAS, including potentially studying the safety and effectiveness of repeat procedures, should they be necessary. Based on regulatory precedent, we believe a PAS may be conducted in parallel with the commercial launch of Revita. If approved, we intend to execute a targeted, efficient go-to market strategy for Revita, driven by a stepwise approach that will build brand awareness, position Revita as a novel and generally well tolerated procedural therapy alternative to escalating insulin therapy, and ultimately expand procedure volume as attempt to validate Revita in endocrine and endoscopy communities as a durable and potentially repeatable option for patients with T2D and other metabolic diseases.

As we progress our Revitalize T2D program and generate clinical evidence in support of Revita, we will invest in building a U.S.-based direct salesforce and medical affairs field team to support our U.S. launch ahead of Revita's potential FDA approval. We will seek to strategically recruit representatives with strong backgrounds and experience in the management of T2D as well as those with a deep understanding of the endoscopist workflow. We expect to grow our field force over time to accelerate broad market adoption of Revita, building on the foundational brand awareness we aim to achieve through our initial educational efforts.

As we generate additional clinical data and insights through our Revitalize T2D program, we plan to carry out an organized medical education effort to inform endocrinologists around the compelling solution provided by our product candidates, as we believe they will serve as the primary prescribing physicians. We believe that the clinical evidence generated from our program will continue to support our messaging to key leaders in the field of endocrinology. We are actively engaging with key thought leaders as we develop and execute on our clinical evidence plan.

If Revita is approved, we intend to commercially launch with the PMA approved console design and plan to submit a supplemental PMA for our next generation commercial console design shortly thereafter. We plan to execute an efficient "hub-and spoke" commercialization strategy to position Revita as a novel procedural therapy to treat T2D and drive its rapid adoption. Leveraging key learnings and insights from our Revitalize T2D program, we plan to have a targeted sales force initially focusing on centers of excellence with metabolically focused endocrinologists and advanced therapeutic endoscopists. We plan to initially target participating physicians from our clinical studies, as we believe their familiarity with our therapies will make them early adopters. Our multi-channel commercialization strategy will include direct marketing campaigns to raise awareness amongst patients for a compelling new treatment alternative in T2D.

We also plan to roll out a robust procedural training and support program for GI endoscopists, ensuring seamless integration of Revita into their workflow. These education and training efforts will be critical in building an installed base in metabolic endoscopy that will begin with providers at large hospitals and expand to outpatient endoscopy centers over time.

Our initial approach will be to focus on T2D patients on long-acting insulin, and progress to patients in earlier stages of T2D and prediabetes and effectively scale within this disease. Once we are established in T2D through clinical validation, medical education and training, strong procedure volumes and a robust installed base, we plan to leverage our foundational platform, technology and core capabilities to expand indications to other serious diseases, including CVD, PCOS and NAFLD, among others.

As we expand the adoption of Revita, we will evaluate potential partnerships and/or distributor relationships for its commercialization in other global geographies. Given the high prevalence and rapidly growing incidence of T2D in certain regions, including Africa, India and China, we believe there is a significant unmet need for a scalable, disease-modifying therapy globally. We plan to pursue regulatory approvals and geographic expansion into additional regions as part of our long-term growth strategy.

Research and Development

We have an experienced research and development team with the scientific, engineering, software, operations and clinical talent that we believe is required to grow our business. We have committed, and expect to continue to commit, significant resources to improve product candidate performance and reliability and reduce

costs. As of March 31, 2022, our research and development team was comprised of 67 employees. For the years ended December 31, 2021 and 2020, we incurred research and development expenses of approximately $26.4 million and $22.4 million, respectively. Major components of the research and development expenses included salaries and benefits, clinical study expenses and production related costs.

We continuously seek to improve Revita, the DMR procedure and our Rejuva gene therapy platform, including improvements in our technology and its accessibility. We believe that technical advantage is important to achieve or sustain a competitive advantage, and therefore our research and development efforts are focused on the continued enhancement of Revita, the DMR procedure and Rejuva. We are dedicated to ongoing innovation with respect to Revita, the DMR procedure, Rejuva, and to expanding our pipeline of product candidates and their applications to treat T2D, prediabetes, and other serious diseases, including CVD, PCOS and NAFLD, among others.

Competition

The medical device and biopharmaceutical industries are characterized by rapid advancement of novel technologies, significant competition and a strong defense of intellectual property rights. While we believe that our product candidates and scientific expertise provides us with competitive advantages, we face competition from multiple sources, including larger and better-funded medical device and biopharmaceutical companies, academic institutions, lifestyle and diet service centers, hospitals, surgical centers, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with currently approved therapies, services and procedures, including lifestyle and diet services, bariatric surgeries, in particular gastric bypass surgeries, and new therapies that may become available in the future. Key factors that would affect our ability to effectively compete with other therapeutics include safety, efficacy, ease of administration, pricing, brand recognition and availability of reimbursement and coverage by third party payors.

There are a number of new classes of agents and combination agents in development for T2D, such as oral GLP-1s and gene therapies, which may offer evidence of significant glycemic improvement and broad metabolic benefit. Pharmaceutical companies are heavily invested in their existing and future product platforms for T2D. They have strong relationships within the clinical community and with prescribing physicians in particular.

Intellectual Property

Our ability to obtain and maintain intellectual property protection for our product candidates and technology is fundamental to the long-term success of our business. We rely on a combination of intellectual property protection strategies, including patents, trademarks, trade secrets, confidentiality policies and procedures, non-disclosure agreements, invention assignment agreements and technical measures designed to protect the intellectual property and commercially valuable confidential information and data used in our business.

As of March 31, 2022, we own: 17 issued U.S. patents; 24 pending U.S. patent applications; six patent cooperation treaty, or PCT, applications that have not entered national stage; 48 issued foreign patents in Australia, Canada, China, Europe, Israel, Japan, Korea, and Russia; and 32 pending foreign patent applications in Australia, Brazil, Canada, China, Europe, Israel, India, Japan, and Korea. The subject matter covered by our owned patents and patent applications include: Revita and components thereof, methods of using Revita, and other exploratory product candidates. Excluding any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, as applicable: our owned issued U.S. patents are expected to expire between January 2032 and June 2037; our owned issued foreign patents are expected to expire between January 2032 and March 2035; any patents that may issue from our owned pending U.S. patent applications are expected to expire between October 2034 and December 2042;

any patents that may issue from our owned pending foreign patent applications or PCT applications are expected to expire between January 2032 and February 2042.

With respect to Revita, as of March 31, 2022, we own 14 issued U.S. patents; 15 pending U.S. patent applications; four PCT applications that have not entered national stage; 41 issued foreign patents in Australia, Canada, China, Europe, Israel, Japan, Korea, and Russia; and 26 pending foreign patent applications in Australia, Brazil, Canada, China, Europe, Israel, India, Japan, and Korea. The issued patents and any patents that may issue from our pending patent applications related to Revita are expected to expire between January 2032 and June 2041, excluding any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, as applicable.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. We cannot be sure that our pending patent applications that we have filed or may file in the future will result in issued patents, and we can give no assurance that any patents that have issued or might issue in the future will protect our current or future products, will provide us with any competitive advantage, and will not be challenged, invalidated, or circumvented.

We intend to pursue additional intellectual property protection to the extent we believe it would be beneficial and cost-effective. Our ability to stop third parties from making, using or commercializing any of our patented inventions will depend in part on our success in obtaining, defending and enforcing patent claims that cover our technology, inventions, and improvements. With respect to our owned intellectual property, we cannot provide any assurance that any of our current or future patent applications will result in the issuance of patents in any particular jurisdiction, or that any of our current or future issued patents will effectively protect any of our product candidates or technology from infringement or prevent others from commercializing infringing products or technology.

Our commercial success depends significantly on our ability to operate without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. The medical device industry is subject to rapid technological change and substantial litigation regarding patent and other intellectual property rights. Numerous third-party patents exist in the fields relating to our product candidates, and it is difficult for industry participants, including us, to identify all third-party patent rights relevant to our product candidates and technologies. We are aware of third-party patents, and patent applications that if issued, may be construed to cover our product candidates or technologies, including Revita.

In addition to our reliance on patent protection for our inventions, products and technologies, we also seek to protect our brand through the procurement of trademark rights. As of March 31, 2022, we own 20 registered trademarks and 21 pending trademark applications for FRACTYL, FRACTYL HEALTH, REVITA, REVITA DMR and other product related brand names in the United States and certain foreign jurisdictions. Furthermore, we rely on trade secrets, know-how, unpatented technology and other proprietary information, to strengthen our competitive position. We have determined that certain technologies, including certain aspects of our software, are better kept as trade secrets. To mitigate the chance of trade secret misappropriation, we enter into non-disclosure and confidentiality agreements with parties who have access to our trade secrets, such as our employees, consultants, advisors and other third parties. We also enter into invention assignment agreements with our employees and consultants that obligate them to assign to us any inventions they have developed while working for us. We generally control access to our proprietary and confidential information through the use of internal and external controls that are subject to periodic review. Although we take steps to protect our proprietary information and trade secrets, third parties may

independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. As a result, we may not be able to meaningfully protect our trade secrets. For further discussion of the risks relating to intellectual property, see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

Manufacturing and Supply

We currently perform final assembly and testing of Revita at our headquarters in Lexington, Massachusetts. We rely upon third-party suppliers for the manufacture of sub-assembly components. We do not have long-term supply agreements with any of our suppliers, some of which are single- or sole-source suppliers. Our purchase order arrangements are terminable at will. We have not yet identified and qualified second-source replacements for many of our critical single-source suppliers. Thus, in the event that our relationship with any of our single- or sole-source suppliers terminates in the future, we may have difficulty maintaining sufficient supplies of key components of our product candidate. Where practicable, we are currently seeking, or intend to seek, second-source manufacturers for our single-source components. We believe that our existing facilities and those of our third-party suppliers are adequate to meet our current manufacturing needs.

Manufacturing facilities that produce medical devices or their component parts are subject to regulation and periodic unannounced inspection by the FDA and other domestic and international regulatory agencies. In the United States, we and some of our sub-assembly component manufacturers will be required to manufacture any products that we sell in compliance with the FDA's Quality System Regulation, or QSR, or the FDA's current good manufacturing practices, or cGMPs, which cover the methods used in, and the facilities used for, the design, testing, control, manufacturing, labeling, quality assurance, packaging, storage and shipping of our product candidates. In international markets, we and some of our sub-assembly component manufacturers are and will be required to obtain and maintain various quality assurance and quality management certifications, and are and will continue to be periodically inspected by international regulatory authorities for certification purposes. We believe our manufacturing operations, and those of our suppliers, are in compliance with applicable regulations of the FDA or other applicable regulatory authorities.

Government Regulation

Our product candidates and our operations are subject to extensive regulation by the FDA and other federal and state authorities in the United States, as well as comparable authorities in foreign jurisdictions. For example, certain of our product candidates are subject to regulation as medical devices in the United States under the Federal Food, Drug, and Cosmetic Act, or FDCA, as implemented and enforced by the FDA, and other product candidates we intend to develop are regulated as biologic-device combination products subject to regulation by the FDA under the FDCA and the Public Health Service Act, or PHSA, and comparable foreign laws and regulations.

United States Regulation of Medical Devices

The FDA regulates the development, design, non-clinical and clinical research, manufacturing, safety, efficacy, labeling, packaging, storage, installation, servicing, recordkeeping, premarket clearance or approval, adverse event reporting, advertising, promotion, marketing and distribution, and import and export of medical devices to ensure that medical devices distributed domestically are safe and effective for their intended uses and otherwise meet the requirements of the FDCA.

FDA Premarket Clearance and Approval Requirements

Unless an exemption applies, each medical device commercially distributed in the United States requires either FDA clearance of a premarket notification submitted under Section 510(k) of the FDCA, classification of FDA's *de novo* classification process or approval of a PMA. Under the FDCA, medical devices

are classified into one of three classes—Class I, Class II or Class III—depending on the degree of risk associated with each medical device and the extent of manufacturer and regulatory control needed to ensure its safety and effectiveness. Class I includes devices with the lowest risk to the patient and are those for which safety and effectiveness can be assured by adherence to the FDA's General Controls for medical devices, which include compliance with the applicable portions of the QSR, establishment registration and device listing, reporting of adverse medical events and certain device malfunctions, known as medical device reporting, or MDR, and truthful and non-misleading labeling, advertising, and promotional materials. Class II devices are subject to the FDA's General Controls, and special controls as deemed necessary by the FDA to ensure the safety and effectiveness of the device. These special controls can include performance standards, post-market surveillance, patient registries and additional labeling requirements.

While most Class I devices are exempt from the 510(k) premarket notification requirement, manufacturers of most Class II devices are required to submit to the FDA a premarket notification under Section 510(k) of the FDCA requesting permission to commercially distribute the device. The FDA's permission to commercially distribute a device subject to a 510(k) premarket notification is generally known as 510(k) clearance. Devices deemed by the FDA to pose the greatest risks, such as life sustaining, life supporting or some implantable devices, or devices that have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally marketed device, are placed in Class III, requiring approval of a PMA. Some pre-amendment devices are unclassified, but are subject to FDA's premarket notification and clearance process in order to be commercially distributed.

510(k) Clearance Marketing Pathway

To obtain 510(k) clearance, the manufacturer must submit to the FDA a premarket notification submission demonstrating that the proposed device is "substantially equivalent" to a legally marketed predicate device. A predicate device is a legally marketed device that is not subject to premarket approval, i.e., a device that was legally marketed prior to May 28, 1976 (pre-amendments device) and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I, or a device that was found substantially equivalent through the 510(k) process. The FDA's 510(k) clearance process usually takes from three to twelve months, but may take longer. The FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence. In addition, FDA collects user fees for certain medical device submissions and annual fees for medical device establishment registration.

If the FDA agrees that the device is substantially equivalent to a predicate device currently on the market, it will grant 510(k) clearance to commercially market the device. If the FDA determines that the device is "not substantially equivalent" to a previously cleared device, the device is automatically designated as a Class III device. The device sponsor must then fulfill more rigorous PMA requirements, or can request a risk-based classification determination for the device in accordance with the "*de novo*" classification process, which is a route to market for novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change or modification in its intended use, will require a new 510(k) clearance or, depending on the modification, PMA approval or grant of a *de novo* request for classification. The FDA requires each manufacturer to determine whether the proposed change requires submission of a 510(k) in the first instance, but the FDA can review any such decision and disagree with a manufacturer's determination. If the FDA disagrees with a manufacturer's determination, the FDA can require the manufacturer to cease marketing and/or request the recall of the modified device until such marketing authorization has been granted. Also, in these circumstances, the manufacturer may be subject to significant regulatory fines or penalties.

Over the last several years, the FDA has proposed reforms to its 510(k) clearance process, and such proposals could include increased requirements for clinical data and a longer review period, or could make it

more difficult for manufacturers to utilize the 510(k) clearance process for their products. For example, in November 2018, FDA officials announced steps that the FDA intended to take to modernize the 510(k) pathway. Among other things, the FDA announced that it planned to develop proposals to drive manufacturers utilizing the 510(k) pathway toward the use of newer predicates. These proposals included plans to potentially sunset certain older devices that were used as predicates under the 510(k) clearance pathway, and to potentially publish a list of devices that have been cleared on the basis of demonstrated substantial equivalence to predicate devices that are more than 10 years old. These proposals have not yet been finalized or adopted, although the FDA may work with Congress to implement such proposals through legislation.

More recently, in September 2019, the FDA issued revised final guidance describing an optional "safety and performance based" premarket review pathway for manufacturers of "certain, well-understood device types" to demonstrate substantial equivalence under the 510(k) clearance pathway by showing that such device meets objective safety and performance criteria established by the FDA, thereby obviating the need for manufacturers to compare the safety and performance of their medical devices to specific predicate devices in the clearance process. The FDA has developed and maintains a list device types appropriate for the "safety and performance based" pathway and continues to develop product-specific guidance documents that identify the performance criteria for each such device type, as well as the testing methods recommended in the guidance documents, where feasible.

PMA Approval Pathway

Revita is a Class III device subject to the requirement for PMA approval. Class III devices require PMA approval before they can be marketed, although some pre-amendment Class III devices for which FDA has not yet required a PMA are cleared through the 510(k) process. The PMA process is more demanding than the 510(k) premarket notification process. In a PMA, the manufacturer must demonstrate that the device is safe and effective, and the PMA must be supported by extensive data, including data from preclinical studies and human clinical trials. The PMA must also contain a full description of the device and its components, a full description of the methods, facilities, and controls used for manufacturing, and proposed labeling. Following receipt of a PMA, the FDA determines whether the application is sufficiently complete to permit a substantive review. If FDA accepts the application for review, it has 180 days under the FDCA to complete its review of a PMA, although in practice, the FDA's review often takes significantly longer, and can take up to several years. An advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. The FDA may or may not accept the panel's recommendation. In addition, the FDA will generally conduct a pre-approval inspection of the applicant or its third-party manufacturers' or suppliers' manufacturing facility or facilities to ensure compliance with the QSR, which set forth cGMPs for devices. PMA applications are also subject to the payment of user fees, which are higher than in the 510(k) process.

The FDA will approve the new device for commercial distribution if it determines that the data and information in the PMA constitute valid scientific evidence and that there is reasonable assurance that the device is safe and effective for its intended use(s). The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution, and collection of long-term follow-up data from patients in the clinical study that supported PMA approval or requirements to conduct additional clinical studies post-approval. The FDA may condition PMA approval on some form of post-market surveillance when deemed necessary to protect the public health or to provide additional safety and efficacy data for the device in a larger population or for a longer period of use. In such cases, the manufacturer might be required to follow certain patient groups for a number of years and to make periodic reports to the FDA on the clinical status of those patients. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of the approval.

Certain changes to an approved device, such as changes in manufacturing facilities, methods, or quality control procedures, or changes in the design performance specifications, which affect the safety or effectiveness of the device, require submission of a PMA supplement. PMA supplements often require submission of the same type of information as a PMA, except that the supplement is limited to information needed to support any changes from

the device covered by the original PMA and may not require as extensive clinical data or the convening of an advisory panel. Certain other changes to an approved device require the submission of a new PMA, such as when the design change causes a different intended use, mode of operation, and technical basis of operation, or when the design change is so significant that a new generation of the device will be developed, and the data that were submitted with the original PMA are not applicable for the change in demonstrating a reasonable assurance of safety and effectiveness. None of our medical device products have been approved through the PMA process.

Clinical Trials

Clinical trials are almost always required to support a PMA and *de novo* request for classification, and are sometimes required to support a 510(k) submission. All clinical investigations of devices to determine safety and effectiveness must be conducted in accordance with the FDA's IDE regulations which govern investigational device labeling, prohibit promotion of the investigational device, and specify an array of recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. If the device presents a "significant risk" to human health, as defined by the FDA, the FDA requires the device sponsor to submit an IDE application to the FDA, which must become effective prior to commencing human clinical trials. If the device under evaluation does not present a significant risk to human health, then the device sponsor is not required to submit an IDE application to the FDA before initiating human clinical trials, but must still comply with abbreviated IDE requirements when conducting such trials. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a patient and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health, or otherwise presents a potential for serious risk to a subject. An IDE application must be supported by appropriate data, such as animal and laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE will automatically become effective 30 days after receipt by the FDA unless the FDA notifies the company that the investigation may not begin. If the FDA determines that there are deficiencies or other concerns with an IDE for which it requires modification, the FDA may permit a clinical trial to proceed under a conditional approval.

Regardless of the degree of risk presented by the medical device, clinical studies must be approved by, and conducted under the oversight of, an Institutional Review Board, or IRB, for each clinical site. The IRB is responsible for the initial and continuing review of the IDE, and may impose additional requirements for the conduct of the study. If an IDE application is approved by the FDA and one or more IRBs, human clinical trials may begin at a specific number of investigational sites with a specific number of patients, as approved by the FDA. If the device presents a non-significant risk to the patient, a sponsor may begin the clinical trial after obtaining approval for the trial by one or more IRBs without separate approval from the FDA, but must still follow abbreviated IDE requirements, such as monitoring the investigation, ensuring that the investigators obtain informed consent, and complying with labeling and record-keeping requirements. In some cases, an IDE supplement must be submitted to, and approved by, the FDA before a sponsor or investigator may make a change to the investigational plan that may affect its scientific soundness, study plan or the rights, safety or welfare of human subjects.

During a study, the sponsor is required to comply with the applicable FDA requirements, including, for example, trial monitoring, selecting clinical investigators and providing them with the investigational plan, ensuring IRB review, adverse event reporting, record keeping and prohibitions on the promotion of investigational devices or on making safety or effectiveness claims for them. The clinical investigators in the clinical study are also subject to FDA's regulations and must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of the investigational device, and comply with all reporting and recordkeeping requirements. Additionally, after a trial begins, the sponsor, the FDA or the IRB could suspend or terminate a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits.

Expedited Development and Review Programs

Following passage of the 21st Century Cures Act, the FDA implemented the Breakthrough Devices Program, which is a voluntary program offered to manufacturers of certain medical devices and device-led

combination products that may provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. The goal of the program is to provide patients and health care providers with more timely access to qualifying devices by expediting their development, assessment and review, while preserving the statutory standards for PMA approval, 510(k) clearance and de novo classification.

The program is available to medical devices that meet certain eligibility criteria, including that the device provides more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, and that the device meets one of the following criteria: (i) the device represents a breakthrough technology, (ii) no approved or cleared alternatives exist, (iii) the device offers significant advantages over existing approved or cleared alternatives, or (iv) the availability of the device is in the best interest of patients. Breakthrough Device designation provides certain benefits to device developers, including more interactive and timely communications with FDA staff, use of postmarket data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design, and prioritized review of premarket submissions.

Post-Market Regulation of Medical Devices

After a product is placed on the market, numerous regulatory requirements continue to apply. These relate to:

- device listing and establishment registration, which helps facilitate FDA inspections and other regulatory action;
- the QSR, which requires manufacturers, including third-party manufacturers, to follow stringent design, validation, testing, control, documentation and other quality assurance procedures during all aspects of the design and manufacturing process;
- labeling regulations, including regulations pertaining to Unique Device Identification, and FDA prohibitions against the promotion of products for uncleared or unapproved use or indication;
- clearance of product modifications for 510(k)-cleared products that could significantly affect safety or effectiveness or that would constitute a major change in intended use or approval of supplemental PMAs for certain changes to an approved device;
- compliance with MDR regulations, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur;
- correction and removal reporting regulations, which require that manufacturers report to the FDA certain corrections and removals;
- post-market restrictions or conditions, including post-market study commitments;
- post-market surveillance regulations, which apply, when necessary, to protect the public health or to provide additional safety and effectiveness data for the medical product;
- the FDA's recall authority, whereby it can ask, or under certain conditions order, device manufacturers to recall from the market a product that is in violation of governing laws and regulations; and
- regulations pertaining to voluntary recalls.

Manufacturing processes for medical devices are required to comply with the applicable portions of the QSR, which cover the methods and the facilities and controls for the design, manufacture, testing, production, processes, controls, quality assurance, labeling, packaging, distribution, installation and servicing of finished devices intended for human use. The QSR also requires, among other things, maintenance of a device master file, device history file, and complaint files. As a manufacturer, we are subject to periodic scheduled and unscheduled inspections by the FDA. Failure to maintain compliance with the QSR requirements could result in the shut-down of, or restrictions on, manufacturing operations and the recall or seizure of marketed products. The discovery of previously unknown problems with any marketed products, including unanticipated adverse events or adverse events of increasing severity or frequency, whether resulting from the use of the device within the scope of its clearance or approval, or off-label by a physician in the practice of medicine, could result in restrictions on the device, including the removal of the product from the market or voluntary or mandatory device recalls.

The FDA has broad regulatory compliance and enforcement powers. If the FDA determines that a manufacturer has failed to comply with applicable regulatory requirements, it can take a variety of compliance or enforcement actions, which may result in any of the following sanctions:

- warning letters, untitled letters, fines, injunctions, consent decrees and civil penalties;
- recalls, withdrawals, or administrative detention or seizure of our products, when and if approved;
- operating restrictions or partial suspension or total shutdown of production;
- refusing or delaying requests for 510(k) clearance, *de novo* classification or PMA approvals of new products or modified products;
- withdrawing PMA approvals that have already been granted;
- refusal to grant export approvals for our products, when and if approved; or
- criminal prosecution.

Advertising and promotion of medical devices, in addition to being regulated by the FDA, are also regulated by the FTC, and by state regulatory and enforcement authorities. Promotional activities for FDA-regulated products of other companies have been the subject of enforcement action brought under healthcare reimbursement laws and consumer protection statutes.

Furthermore, under the federal U.S. Lanham Act and similar state laws, competitors and others can initiate litigation relating to advertising claims. In addition, we are required to meet regulatory requirements in countries outside the United States, which can change rapidly with relatively short notice.

United States Regulation of Biologics and Combination Biologic/Device Products

In the United States, biological products, or biologics, such as those gene therapy candidates we intend to develop through our proprietary Rejuva gene therapy platform, are subject to regulation under the FDCA, PHSA, and other federal, state, local and foreign statutes and regulations.

Combination Biologic/Device Products

We expect our gene therapy candidates developed through our Rejuva gene therapy platform to be subject to regulation in the United States as combination products comprised of a biologic product candidate and a device delivery system. A combination product is the combination of two or more regulated components, such as biologic/device, that are combined or mixed and produced as a single entity, packaged together in a single

package or as a unit or a biologic or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified biologic or device where both are required to achieve the intended use, indication or effect. If marketed individually, each component would be subject to different regulatory pathways and would require approval of independent marketing applications by the FDA – one for the device component and one for the biologic component of the combination.

A combination product, however, is assigned to a center within FDA that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. To determine which FDA center or centers will review a combination product candidate submission, companies may submit a request for assignment to the FDA. Those requests may be handled formally or informally. In some cases, jurisdiction may be determined informally based on FDA experience with similar products. However, informal jurisdictional determinations are not binding on the FDA. Companies also may submit a formal Request for Designation to the FDA Office of Combination Products. The Office of Combination Products will review the request and make its jurisdictional determination within 60 days of receiving a Request for Designation.

In the case of our Rejuva gene therapy candidates, we believe that the primary mode of action will be attributable to the biologic component of the combination product. We therefore would expect to seek approval of any such combination biologic/device product candidate through a single Biologics License Application, or BLA, and we do not expect that the FDA will require a separate marketing authorization for the device component.

U.S. Biologics Regulation

The process required by the FDA before biologics may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements, or GLPs;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical trials may begin;
- approval by an IRB or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended use in accordance with good clinical practice requirements, or GCPs;
- preparation of and submission to the FDA of a BLA, after completion of all pivotal clinical trials and other necessary studies;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMPs (including the QSR in the case of the device component of any biologic/device combination product), and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and

- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

The preclinical developmental stage generally involves laboratory evaluations of chemistry, formulation and stability, as well as studies to evaluate the product candidate's toxicity in animals, in an effort to support subsequent clinical testing. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations.

Prior to beginning the first clinical trial with a product candidate in the United States, the trial sponsor must submit an IND to the FDA. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product candidate, chemistry, manufacturing, and controls information, and any available human data or literature to support the use of the product candidate. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In addition to the IND submission process, under the National Institutes of Health, or NIH, Guidelines for Research Involving Recombinant DNA Molecules, or the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring subject safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments.

Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study, and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries, including clinicaltrials.gov.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may also be made a condition to approval of the BLA.

While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

In addition, during the development of a new biologic, sponsors are given opportunities to meet with the FDA at certain points, including prior to submission of an IND, at the end of Phase 2, and before a BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach alignment on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the product candidate.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA

as part of a BLA requesting approval to market the product candidate for one or more indications. The BLA must include all relevant data available from preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product candidate, or from a number of alternative sources, including studies initiated by independent investigators. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether the product candidate is safe, pure and potent for the proposed indication, and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may also convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may include limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate

controls and specifications. Once a BLA is approved, the FDA may withdraw such approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety, purity and potency after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the fast track program is intended to expedite or facilitate the process for developing and reviewing product candidates that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a fast track-designated product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. A fast track-designated product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a biologic product candidate submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A BLA is eligible for priority review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review).

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements

Biologics are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon them. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved label to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims that are in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict a manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Affordable Care Act, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product.

Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. Whether products deemed "interchangeable" by the FDA are readily substituted by pharmacies is governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

Foreign Government Regulation

In addition to U.S. regulations, we are subject to a variety of foreign government regulations applicable to medical devices, medicinal products and combination products.

Regulation of Medical Devices in the European Union

The EU has adopted specific directives and regulations regulating the design, manufacture, clinical investigation, conformity assessment, labeling and adverse event reporting for medical devices.

Until May 25, 2021, medical devices were regulated by the Council Directive 93/42/EEC or Medical Devices Directive, which has been repealed and replaced by Regulation (EU) No 2017/745, or Medical Devices Regulation. Our current certificates have been granted and renewed under the Medical Devices Directive whose regime is described below. However, as of May 26, 2021, some of the Medical Devices Regulation requirements apply in place of the corresponding requirements of the Medical Devices Directive with regard to registration of economic operators and of devices, post-market surveillance, market surveillance and vigilance requirements. Pursuing marketing of medical devices in the EU will notably require that our devices be certified under the new regime set forth in the Medical Devices Regulation when our current certificates expire, one expiring on May 26, 2024 and the other on September 30, 2023.

Medical Devices Directive

Under the Medical Devices Directive, all medical devices placed on the market in the EU must meet the relevant essential requirements laid down in Annex I to the Medical Devices Directive, including the requirement that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performance intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner. The European Commission has adopted various standards applicable to medical devices. These include standards governing common requirements, such as sterilization and safety of medical electrical equipment and product standards for certain types of medical devices. There are also harmonized standards relating to design and manufacture. While not mandatory, compliance with these standards is viewed as the easiest way to satisfy the essential requirements as a practical matter as it creates a rebuttable presumption that the device satisfies that essential requirement.

To demonstrate compliance with the essential requirements laid down in Annex I to the Medical Devices Directive, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. As a general rule, demonstration of conformity of medical devices and their manufacturers with the essential requirements must be based, among other things, on the evaluation of clinical data supporting the safety and performance of the products during normal conditions of use. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-declare the conformity of its products with the essential requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a notified body. Notified bodies are independent organizations designated by EU member states to assess the conformity of devices before being placed on the market. A notified body would typically audit and examine a product's technical dossiers and the manufacturers' quality system (the notified body must presume that quality systems which implement the relevant harmonized standards – which is ISO 13485:2016 for Medical Devices Quality Management Systems – conform to these requirements). If satisfied that the relevant product conforms to the relevant essential requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE Mark to the device, which allows the device to be placed on the market throughout the EU.

Throughout the term of the certificate of conformity, the manufacturer will be subject to periodic surveillance audits to verify continued compliance with the applicable requirements. In particular, there will be a new audit by the notified body before it will renew the relevant certificate(s).

Medical Devices Regulation

The regulatory landscape related to medical devices in the EU recently evolved. On April 5, 2017, the Medical Devices Regulation was adopted with the aim of ensuring better protection of public health and patient

safety. The Medical Devices Regulation, among other things, establishes a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. Unlike the Medical Devices Directive, the Medical Devices Regulation is directly applicable in EU member states without the need for member states to implement into national law. This aims at increasing harmonization across the EU.

The Medical Devices Regulation became effective on May 26, 2021. The new Regulation among other things:

- strengthens the rules on placing devices on the market (e.g. reclassification of certain devices and wider scope than the Medical Devices Directive) and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- establishes explicit provisions on importers' and distributors' obligations and responsibilities;
- imposes an obligation to identify a responsible person who is ultimately responsible for all aspects of compliance with the requirements of the new regulation;
- improves the traceability of medical devices throughout the supply chain to the end-user or patient through the introduction of a unique identification number, to increase the ability of manufacturers and regulatory authorities to trace specific devices through the supply chain and to facilitate the prompt and efficient recall of medical devices that have been found to present a safety risk;
- sets up a central database (EUDAMED) to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk devices, such as implants, which may have to undergo a clinical evaluation consultation procedure by experts before they are placed on the market.

Devices lawfully placed on the market pursuant to the Medical Devices Directive prior to May 26, 2021 may generally continue to be made available on the market or put into service until May 26, 2025, provided that the requirements of the transitional provisions are fulfilled. In particular, the certificate in question must still be valid. However, even in this case, manufacturers must comply with a number of new or reinforced requirements set forth in the Medical Devices Regulation, in particular the obligations described below.

The Medical Devices Regulation requires that before placing a device, other than a custom-made device, on the market, manufacturers (as well as other economic operators such as authorized representatives and importers) must register by submitting identification information to the electronic system (EUDAMED), unless they have already registered. The information to be submitted by manufacturers (and authorized representatives) also includes the name, address and contact details of the person or persons responsible for regulatory compliance. The new Regulation also requires that before placing a device, other than a custom-made device, on the market, manufacturers must assign a unique identifier to the device and provide it along with other core data to the unique device identifier, or UDI, database. These new requirements aim at ensuring better identification and traceability of the devices. Each device – and as applicable, each package – will have a UDI composed of two parts: a device identifier, or UDI-DI, specific to the manufacturer and the device, and a production identifier, or UDI-PI, to identify the unit of device production. Manufacturers are also notably responsible for entering the necessary data on EUDAMED, which includes the UDI database, and for keeping it up to date. EUDAMED is not yet fully functional; however, all EUDAMED modules are currently expected to be available from May 2022.

All manufacturers placing medical devices on the market in the EU must comply with the EU medical device vigilance system which has been reinforced by the Medical Devices Regulation. Under this system, serious incidents and Field Safety Corrective Actions , or FSCAs must be reported to the relevant authorities of the EU member states. These reports will have to be submitted through EUDAMED – once functional – and aim to ensure that, in addition to reporting to the relevant authorities of the EU member states, other actors such as the economic operators in the supply chain will also be informed. Until EUDAMED is fully functional, the corresponding provisions of the Medical Devices Directive continue to apply. A serious incident is defined as any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect, which, directly or indirectly, might have led or might lead to the death of a patient or user or of other persons or to a temporary or permanent serious deterioration of a patient's, user's or other person's state of health or a serious public health threat. Manufacturers are required to take FSCAs defined as any corrective action for technical or medical reasons to prevent or reduce a risk of a serious incident associated with the use of a medical device that is made available on the market. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device. FSCAs must be communicated by the manufacturer or its legal representative to its customers and/or to the end users of the device through Field Safety Notices. For similar serious incidents that occur with the same device or device type and for which the root cause has been identified or a FSCA implemented or where the incidents are common and well documented, manufacturers may provide periodic summary reports instead of individual serious incident reports.

Among the new requirements, manufacturers (and authorized representatives) must have available within their organization at least one person responsible for regulatory compliance, or PRRC, who possesses the requisite expertise in the field of medical devices. The PRRC is notably responsible for compliance with post-market surveillance and vigilance requirements.

The advertising and promotion of medical devices is subject to some general principles set forth in EU legislation. According to the Medical Devices Regulation, only devices that are CE-marked may be marketed and advertised in the EU in accordance with their intended purpose. Directive 2006/114/EC concerning misleading and comparative advertising and Directive 2005/29/EC on unfair commercial practices, while not specific to the advertising of medical devices, also apply to the advertising thereof and contain general rules, for example, requiring that advertisements are evidenced, balanced and not misleading. Specific requirements are defined at a national level. EU member states' laws related to the advertising and promotion of medical devices, which vary between jurisdictions, may limit or restrict the advertising and promotion of products to the general public and may impose limitations on promotional activities with healthcare professionals.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU Member States plus Norway, Liechtenstein and Iceland.

Brexit

From January 1, 2021 onwards, the Medicines and Healthcare Products Regulatory Agency, or MHRA, becomes the sovereign regulatory authority responsible for the Great Britain (i.e. England, Wales and Scotland) medical device market according to the requirements provided in the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) that sought to give effect to the three pre-existing EU directives governing active implantable medical devices, general medical devices and in vitro diagnostic medical devices whereas, broadly, Northern Ireland continues to be governed by EU rules according to the Northern Ireland Protocol. Following the end of the Brexit transitional period on January 1, 2021, new regulations require medical devices to be registered with the MHRA (but manufacturers will be given a grace period of four to 12 months to comply with the new registration process, depending on the classification of the device) before being placed on the Great Britain market. The MHRA will only register devices where the manufacturer or their United Kingdom Responsible Person has a registered place of business in the United Kingdom. Manufacturers based outside the United Kingdom will need to appoint a U.K. Responsible Person that has a registered place of business in the United

Kingdom to register devices with the MHRA in line with the grace periods. By July 1, 2023, in Great Britain, all medical devices will require a UKCA, or UK Conformity Assessed, mark but CE marks issued by EU notified bodies will remain valid until this time. Manufacturers may choose to use the UKCA mark on a voluntary basis until June 30, 2023. However, UKCA marking will not be recognized in the EU. The rules for placing medical devices on the market in Northern Ireland, which is part of the United Kingdom, differ from those in the rest of the United Kingdom. Compliance with this legislation is a prerequisite to be able to affix the UKCA mark to our products, when and if approved, without which they cannot be sold or marketed in Great Britain.

In addition, the Trade Deal between the United Kingdom and the EU generally provides for cooperation and exchange of information between the parties in the areas of product safety and compliance, including market surveillance, enforcement activities and measures, standardization-related activities, exchanges of officials, and coordinated product recalls. As such, processes for compliance and reporting should reflect requirements from regulatory authorities.

Coverage and Reimbursement

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific product lines and procedures. In the EU and UK, member states impose controls on whether products are reimbursable by national or regional health service providers and on the prices at which devices are reimbursed under state-run healthcare schemes. More and more, local, product specific reimbursement law is applied as an overlay to Medical Devices Regulation, which has provided an additional layer of clearance requirement.

Regulation of Medicinal Products in the European Union

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies, commercial sales, and distribution of our future products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries. In addition, ethical, social and legal concerns about gene-editing technology, gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use.

Most countries outside of the United States, including the EU, require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In addition, whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approval from comparable regulatory authorities outside the United States before we can commence clinical studies or marketing of the product candidate in those countries. The requirements and process governing the conduct of clinical trials, approval, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-Clinical Studies and Clinical Trials

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on good clinical practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Certain countries outside of the United States, including the EU, have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. A clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved by the national health authority and the ethics committee has granted a positive opinion in relation to the conduct of the trial in the relevant member state(s), in accordance with a country's requirements, clinical study development may proceed.

The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, CTAs must be submitted to the competent authority in each EU member state in which the trial will be conducted. Under the new Regulation on Clinical Trials, which will become applicable on 31 January 2022, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only limited involvement. Any substantial changes to the trial protocol or other information submitted with the CTA must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorizations

In order to market our future product candidates in the EU, and in many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of a product candidate (including an investigational biological product) under EU regulatory systems, we must submit a marketing authorization application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product.

There are two types of MAs:

- "Centralized MA" is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the EU. It is compulsory for certain types of products, such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) advanced-therapy medicinal products, or ATMPs, such as gene therapy, somatic cell-therapy or tissue-engineered medicines and (iv) medicinal products containing a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for any other medicinal products containing new active substances not authorized in the EU or for product candidates which constitute a significant therapeutic, scientific, or technical innovation or for which the granting of authorization would be in the interests of public health in the EU.

- "National MAs," which are issued by the competent authorities of the EU member states and only cover their respective territory, are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in

an EU member state, this national MA can be recognized in another member state through the Mutual Recognition Procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the Reference member state.

The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a MAA is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and/or are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance. Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "normal" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases

or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

Data and Marketing Exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving MA, reference product candidates generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAA must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Brexit

The United Kingdom left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the United Kingdom during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, or TCA, which became provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition cGMP inspections of manufacturing facilities for medicinal products and cGMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. While the TCA has avoided a “no deal” Brexit scenario, and provides for quota and tariff free trading of goods in principle, it is nevertheless expected that the TCA will result in the creation of non-tariff barriers (such as increased shipping and regulatory costs and complexities) to the trade in goods between the UK and EU. Further, the TCA does not provide for the continued free movement of services between the United Kingdom and EU and also grants each of the United Kingdom and EU the ability, in certain circumstances, to unilaterally impose tariffs on one another.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU Clinical Trial Regulation (Regulation (EU) No 536/2014) or in relation to orphan medicines will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ‘appropriate authority’ to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the MHRA, is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland Protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, or GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019 (the Exit Regulations).

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

For MAs, an applicant for a centralized MA must be established in the EU. After Brexit, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (Centralized Procedure) MA when determining an application for a Great Britain authorization until December 31, 2022; or use the MHRA's Decentralized or Mutual Recognition Procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

The full impact of such arrangements are expected to become clearer in the course of 2021 and 2022.

Coverage and Reimbursement

In some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing product pricing vary widely from country to country. For example, in the EU pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU member states' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and can control the prices and reimbursement levels of medicinal products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Even if approved for reimbursement, historically, product candidates launched in some foreign countries, such as some countries in the EU, do not follow price structures of the United States and prices generally tend to be significantly lower.

Other Healthcare Laws

Healthcare Fraud and Abuse Laws

In the United States, we are subject to a number of federal and state healthcare regulatory laws that restrict business practices in the healthcare industry. These laws include, but are not limited to, federal and state anti-kickback, false claims, transparency and other healthcare fraud and abuse laws.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including cash, improper discounts, and free or reduced price items and services. Among other things, the Anti-Kickback Statute has been interpreted to apply to arrangements between medical device manufacturers on the one hand and prescribers and purchasers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution,

the exceptions and safe harbors are drawn narrowly. The government can exercise enforcement discretion in taking action against unprotected activities. Further, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The majority of states also have anti-kickback laws, which establish similar prohibitions, and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers and self-pay patients.

The federal false claims laws, including the civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Actions under the civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Moreover, a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. In addition, various states have enacted false claim laws analogous to the federal False Claims Act, although many of these state laws apply where a claim is submitted to any third-party payor and not merely a federal healthcare program.

The federal Health Insurance Portability and Accountability Act of 1996 created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, such obligations will include payments and other transfers of value provided in the previous year to additional healthcare professionals, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives.

Violations of fraud and abuse laws, including federal and state anti-kickback and false claims laws, may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees of such companies.

Coverage and Reimbursement

Significant uncertainly exists as to the coverage and reimbursement status of procedures using any product candidates for which we may obtain regulatory approvals. In the United States, sales of our product candidates, if approved, will depend, in part, on the extent to which governmental authorities, private health

insurers and other third-party payors provide coverage for and establish adequate reimbursement levels for the procedures in which our product candidates, if approved, are used. In the United States, third-party payors include federal and state healthcare programs, private managed care plans, health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for procedures using our products will be available from government health administration authorities, private insurers and other organizations. Coverage and reimbursement by governmental and other third-party payors may depend upon a number of factors, including the third-party payor's determination that use of a product or service and its use for a particular patient is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that coverage and reimbursement will be available for any procedure that uses our product candidate that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which a product candidate is approved by the FDA or comparable foreign regulatory authorities. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical devices and medical services, in addition to questioning their safety and efficacy. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained.

No uniform policy of coverage and reimbursement among payors in the United States exists and coverage and reimbursement for procedures can differ significantly from payor to payor. Moreover, the process for determining whether a third-party payor will provide coverage for a product or procedure may be separate from the process for establishing the reimbursement rate that such a payor will pay for the procedure using new medical devices and technology. A payor's decision to provide coverage for a procedure does not imply that an adequate reimbursement rate will be approved to also cover the cost of our product candidates, if approved. Further, one payor's determination to provide coverage for a product or procedure does not assure that other payors will also provide coverage for the product or procedure. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to ensure profitability.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific product lines and procedures. In the European Union, member states are facing increased pressure to limit public healthcare spending. There can be no assurance that procedures using our product candidates, once approved, will be covered for a specific indication or will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidate profitably, once approved. More and more, local, product specific reimbursement law is applied as an overlay to Medical Devices Regulation, which has provided an additional layer of clearance requirement.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes in the United States has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly medical devices and surgical procedures and other treatments, has become very intense. Coverage policies and third- party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates profitably, if approved. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. Current and future legislative proposals to further reform healthcare or reduce healthcare costs may limit coverage of or lower reimbursement for the procedures associated with the use of our products, when and if approved. The cost containment measures that payors and providers are instituting and the effect of any healthcare reform initiative implemented in the future could impact our revenue from the sale of our future products.

The implementation of the Affordable Care Act, or ACA, in the United States, for example, has changed healthcare financing and delivery by both governmental and private insurers substantially, and affected medical device manufacturers significantly. The ACA, among other things, provided incentives to programs that increase the federal government's comparative effectiveness research, and implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models. Additionally, the ACA expanded eligibility criteria for Medicaid programs and created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. Since its enactment, there have been judicial, executive and political challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law, including the TCJA, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a United States District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the United States Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. In June 2021, the United States Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, upholding the ACA. It is unclear how any challenge to repeal or replace the ACA will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, reduced Medicare payments to providers by 2% per fiscal year, effective on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. Additionally, the American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to

five years. The Medicare Access and CHIP Reauthorization Act of 2015 repealed the formula by which Medicare made annual payment adjustments to physicians and replaced the former formula with fixed annual updates and a new system of incentive payments that began in 2019 that are based on various performance measures and physicians' participation in alternative payment models, such as accountable care organizations.

We expect additional state and federal healthcare reform measures to be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our future products or additional pricing pressure.

European Healthcare Laws

Many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medical devices and medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities. In addition, many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on manufacturers. Certain countries also mandate implementation of commercial compliance programs.

Data Privacy & Security

Numerous state, federal and foreign laws, regulations, and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, including clinical trial data, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. For example, the GDPR imposes strict requirements for processing the personal data of individuals within the European Economic Area. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Further, from January 1, 2021, companies have had to comply with the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Facilities

Since 2016, our corporate headquarters has been located at 17 Hartwell Avenue Lexington, Massachusetts 02421, where we currently lease approximately 30,000 square feet of office and manufacturing space. As of March 31, 2022, approximately 67 of our employees are located at our corporate headquarters.

Human Capital

As of March 31, 2022, we have 83 full-time employees, 67 of whom are dedicated to research and development, and 11 of our employees hold doctorate degrees (i.e., Ph.D., Pharm.D. or M.D.). None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for

equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives, including health care, retirement planning and paid time off.

We believe that much of our success is rooted in the diversity of our teams and our commitment to inclusion. We value diversity at all levels and focus on extending our diversity and inclusion initiatives across our entire workforce.

Legal Proceedings

We are not subject to any material legal proceedings.

MANAGEMENT

The following table provides information regarding our executive officers and members of our board of directors (ages as of the date of this prospectus):

Name	Age	Position(s)
Executive Officers		
Harith Rajagopalan, M.D., Ph.D.	45	Co-Founder, President, Chief Executive Officer, Director
Jay D. Caplan	60	Co-Founder, Chief Product Officer
Lisa A. Davidson	55	Chief Financial Officer, Treasurer
Juan Carlos Lopez-Talavera, M.D., Ph.D.	60	Chief Medical Officer
Non-Employee Directors		
Kelly Barnes	56	Director
William W. Bradley	78	Director
Brian Dovey	79	Director
Marc Elia	46	Director
Clive Meanwell, M.B., Ch.B., M.D.	64	Director
Ajay Royan	42	Director
Amy W. Schulman	61	Director
Allan R. Will	68	Chairman

Executive Officers

Harith Rajagopalan, M.D. Ph.D. Dr. Rajagopalan co-founded Fractyl in 2010 and has served as our Chief Executive Officer and a member of our board of directors since 2011, and our President since January 2022, while serving as an Entrepreneur-in-Residence at General Catalyst Partners from 2009 to 2011. Prior to founding Fractyl, Dr. Rajagopalan trained in internal medicine and clinical cardiology at Brigham and Women's Hospital in Boston, Massachusetts from 2005 to 2011, and completed a research fellowship at Harvard Medical School from 2009 to 2011. Dr. Rajagopalan received his B.S. in chemistry from Stanford University, and his M.D. and Ph.D. from Johns Hopkins University School of Medicine. We believe that Dr. Rajagopalan is qualified to serve on our board of directors due to his role as co-founder of Fractyl Health, his management experience as our Chief Executive Officer and his scientific and medical experience.

Jay D. Caplan. Mr. Caplan co-founded Fractyl in 2010 and has served as our Chief Product Officer since January 2022, a member of our board of directors from 2011 to 2017 and previously served as our President from 2011 until January 2022. Prior to founding Fractyl, Mr. Caplan served as Chief Operating Officer of Candela Corporation from November 2007 to January 2010, which was then a publicly held U.S.-based global medical aesthetic device company. Prior to Candela, he served as Chief Technology Officer and Vice President of Research and Development of InfraReDx, Inc. from September 2001 to October 2007, a privately held company that designs and develops catheter-based coronary imaging devices, that was later acquired by Nipro Corporation (Japan). Mr. Caplan also previously served as Vice President of Operations of Thermo Cardiosystems Inc. (now part of Abbott Laboratories), where he assisted in developing the HeartMate II left ventricular assist device. Mr. Caplan received his B.S. in electrical engineering from the Massachusetts Institute of Technology, or MIT, and his M.B.A. from the University of Pennsylvania's Wharton School of Business.

Lisa A. Davidson. Ms. Davidson has served as our Chief Financial Officer and Treasurer since August 2015. Prior to joining us, Ms. Davidson was Vice President of Finance and Administration of Flexion Therapeutics, Inc., or Flexion, a publicly held biopharmaceutical company focused on the development and commercialization of novel, injectable pain therapies, from March 2009 to August 2015. Prior to Flexion, Ms. Davidson served as Director of Finance of OmniSonics Medical Technologies, Inc., a privately held U.S.-based medical device company focused on the treatment of vascular occlusive diseases. Ms. Davidson also

previously served as Director of Finance of PerkinElmer Inc., a publicly held company focused on globally providing products and services to customers in health sciences and other advanced technology markets, and as Director of Finance at Citizens Advisers, Inc., an investment adviser to Citizens Funds, an investment company. Ms. Davidson received her B.A. and M.B.A. from the University of New Hampshire.

Juan Carlos Lopez-Talavera, M.D. Ph.D. Dr. Lopez-Talavera has served as our Chief Medical Officer since March 2019. Prior to joining us, Dr. Lopez-Talavera served as Chief Medical Officer at Enterome from January 2018 to December 2018, a clinical-stage biopharmaceutical company developing microbiome-based therapies for immune-mediated diseases. Prior to Enterome, Dr. Lopez-Talavera served as Executive Vice President at Intercept Pharmaceuticals, a biopharmaceutical company focusing on the development of novel synthetic bile acid analogs to tread chronic liver diseases, from June 2015 to December 2017. In addition, he was Assistant Professor of Medicine at the University of Pittsburg School of Medicine where he was in charge of the experimental program for pancreatic islet cell transplantation and gene therapy. Dr. Lopez-Talavera received his M.D. and Ph.D. in molecular biology and virology at Universitat Autonoma Barcelona, and completed his Post-Doctoral Fellowship at Yale University, focusing on liver, splanchnic and cardiovascular physiology.

Non-Employee Directors

Kelly Barnes. Ms. Barnes has served as a member of our board of directors since January 2022. Prior to joining us, she served in various roles at PricewaterhouseCoopers from 1988 to 2020, most recently serving as a Global Health Industries Leader from 2018 to 2020 and as a U.S. Health Industries Leader from 2009 to 2020, where she oversaw services across all health-related industries. Ms. Barnes currently serves on the board of directors of Included Health and is a member of the executive advisory board of the Walton College of Business at the University of Arkansas. She received her B.S.B.A. and M.S.A in accounting from the University of Arkansas and is a registered certified public accountant in the state of Texas. We believe that Ms. Barnes is qualified to serve on our board of directors due to her strong business and financial acumen, and extensive experience advising companies in the healthcare industry.

William W. Bradley. Senator Bradley has served as a member of our board of directors since March 2017. Since 2000, Sen. Bradley has been a managing director of Allen & Company LLC, an investment banking firm. From 2001 until 2004, he acted as chief outside advisor to McKinsey & Company's non-profit practice. In 2000, Sen. Bradley was a candidate for the Democratic nomination for President of the United States. He served as a senior advisor and vice chairman of the International Council of JP Morgan & Co. from 1997 through 1999. During that time, Sen. Bradley also worked as an essayist for CBS Evening News, and as a visiting professor at Stanford University, the University of Notre Dame and the University of Maryland. Sen. Bradley served in the U.S. Senate from 1979 until 1997, representing the State of New Jersey. Prior to serving in the U.S. Senate, he was an Olympic gold medalist in 1964, and from 1967 through 1977 he played professional basketball for the New York Knicks, during which time they won two world championships. Sen. Bradley previously served on the board of directors of Starbucks Corporation from June 2003 until March 2018. Sen. Bradley also previously served on the board of directors of Seagate Technology, Willis Group Holdings Limited and QuinStreet, Inc. Sen. Bradley received his B.A. in American history from Yale University and his M.A. in political philosophy and economics from the University of Oxford, Worcester College, where he was a Rhodes Scholar. We believe that Mr. Bradley is qualified to serve on our board of directors due to his deep understanding of public policy and U.S. governmental and regulatory affairs, and his broad leadership and corporate governance experience.

Brian Dovey. Mr. Dovey has served as a member of our board of directors since May 2016. Mr. Dovey has also served as a member of the Board of Directors of DRI Holdings Limited, a real estate investment company, since 2012, NovaMedica, a Russian pharmaceutical company, since 2012, WindMIL Therapeutics, Inc., a clinical-stage biotechnology company using bone marrow insights to develop cell therapies for cancer patients, since 2016, and Nobias Therapuetics Inc., a developer of pediatric disease drugs, since 2020. Mr. Dovey has previously served as a director at over 35 companies, both public and private, and has sat on a number of

Compensation, Audit, Pricing and Governance/Nominating Committees. Mr. Dovey is also a Managing Member of Domain Associates, LLC. Mr. Dovey received his B.A. in mathematics from Colgate University and his M.B.A. from Harvard Business School. We believe that Mr. Dovey is qualified to serve on our board of directors due to his extensive experience working with and serving on the boards of directors of various pharmaceutical, healthcare and other companies.

Marc Elia. Mr. Elia has served as a member of our board of directors since June 2021. Mr. Elia also serves as a director and audit committee member at SQZ Biotech, a clinical-stage biotechnology company developing cell therapies for patients with cancer, and previously served as a director at Adimab LLC, a provider of therapeutic antibody discovery and engineering technologies, and at Adagio Therapeutics, a biotechnology firm developing antibodies against viruses, including potentially against COVID-19. Mr. Elia also founded M28 Capital Management, a healthcare sector investment fund, and serves as its Chief Investment Officer. Mr. Elia received his B.A. at Carleton College, graduating with magna cum laude honors. We believe that Mr. Elia is qualified to serve on our board of directors due to his business expertise and experience serving as a director at various life science companies.

Clive Meanwell, M.B., Ch.B., M.D. Dr. Meanwell has served as a member of our board of directors since June 2021. Dr. Meanwell has also been a director and member of the compensation and audit committees at BB Biotech, a publicly-held Switzerland-based biotechnology investment company, since 2004, a director at EQRx, a privately-held biotechnology company aiming to make medicine more affordable, since 2020, a director at Comanche BioPharma, a privately-held preclinical biopharmaceutical company developing treatments for preeclampsia, since 2021 and a director at Hugo Health, a privately-held cloud-based healthcare platform, since 2021. Dr. Meanwell currently also serves at Executive Chairman and General Partner at Population Health Partners LP, an investment company focused on innovative therapeutics with the potential to transform health outcomes for populations. Dr. Meanwell also founded The Medicines Company, a biopharmaceutical company focused on addressing cardiovascular disease, and served as Executive Chairman and Chief Executive Officer until 2018 and Chief Innovation Officer until 2020. Dr. Meanwell received his M.B., Ch.B. and M.D. from the University of Birmingham, UK. We believe that Dr. Meanwell is qualified to serve on our board of directors due to his medical background and experience working with and serving on the boards of directors of various pharmaceutical and healthcare companies.

Ajay Royan. Mr. Royan has served as a member of our board of directors since 2014. Mr. Royan has served as Managing General Partner at Mithril Capital Management LLC, or Mithril, a venture capital firm investing in technology companies, since June 2012 and on the board of directors of several private companies in which Mithril Capital Management LLC or its affiliates have invested. Mr. Royan has served as a director of Adimab, LLC since September 2014, has served as a director of Adagio Therapeutics since October 2020 and has served on the board of Neocis, Inc. Previously, Mr. Royan served on the board of Auris Health. Mr. Royan serves on the science advisory board of the Oak Ridge National Laboratory, the board of directors of Fulbright Canada, and the Presidents' Circle of the National Academies of Science, Engineering and Medicine. Mr. Royan received his B.A. from Yale University. We believe that Mr. Royan is qualified to serve on our board of directors due to his experience working in the venture capital industry and experience working with and serving on the boards of directors of numerous technology companies.

Amy W. Schulman. Ms. Schulman has served as a member of our board of directors since September 2018. Ms. Schulman is a healthcare investor and Managing Partner at Polaris Partners and co-founded and acts as Managing Partner of the Polaris Innovation Fund, which was formed in 2017. Ms. Schulman currently serves as Executive Chair of SQZ Biotech, as well as Lyndra Therapeutics, which she co-founded and served as the company's initial Chief Executive Officer from July 2015 to September 2019. Prior to joining Polaris Partners, Ms. Schulman, held various executive roles at Pfizer, including General Counsel, President of Pfizer Consumer Healthcare and Pfizer Nutrition. Ms. Schulman is currently a member of the board of directors of Alnylam Pharmaceuticals and Mount Sinai Hospital, and also serves as a member of Singapore's Health and Biomedical Sciences International Advisory Council. She previously served as a Senior Lecturer at Harvard Business School and was a partner at DLA Piper. Ms. Schulman received her B.A. in Philosophy and English at Wesleyan

University, graduating with Phi Beta Kappa honors, and her J.D. from Yale Law School. We believe that Ms. Schulman is qualified to serve on our board of directors due to her experience working with and serving on the boards of directors of various pharmaceutical and healthcare companies.

Allan R. Will. Mr. Will has served as Chairman of our board of directors since August 2012. Mr. Will has also served as Chairman, President and Chief Executive Officer of EBR Systems, Inc., a privately held company developing a wireless cardiac pacing system for heart failure, from October 2011 to June 2019, and as Executive Chair since June 2019. He also serves as Chair of the board of directors of SetPoint Medical, Inc., a privately held clinical-stage bioelectronics medicine company dedicated to treating patients with chronic autoimmune disease, since March 2011. Since 2014, he has served as a director of Fogarty Innovation, a not-for-profit organization dedicated to advancing human health worldwide. Prior to these roles, Mr. Will served as founding Managing Director of Split Rock Partners' (and its predecessor, St. Paul Venture Capital's) Silicon Valley venture capital office, focusing on the therapeutic medical device field. Previously, Mr. Will founded The Foundry, an incubator dedicated to transforming medical device concepts into companies, where he also served as Chair and Chief Executive Officer from 1998 to 2002 and Chair until 2010, co-founding eleven companies including, among others, Ardian, Inc., a medical device company focused on treating hypertension, which was subsequently acquired by Medtronic plc, and Evalve Inc., a company treating heart failure by repairing mitral valves percutaneously, now a wholly owned subsidiary of Abbott Laboratories. Mr. Will is an inventor on more than 30 issued patents, is a University of Maryland Distinguished Alumnus and a recipient of the ASTIA/Deloitte Excellence in Mentoring Women Executives Award. He served on the MIT Entrepreneurship Center Shareholders' Board and the University of Maryland President's Committee on Innovation and Entrepreneurship. Mr. Will received his M.S. in management from MIT and his B.S. in zoology from the University of Maryland. We believe that Mr. Will is qualified to serve on our board of directors due to his experience as a founder, senior executive and board member of numerous life science companies.

Family Relationships

There are no family relationships among any of our directors or executive officers.

Composition of our Board of Directors

Our board of directors currently consists of nine directors. Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the number of directors on our board of directors will be fixed from time to time by resolution of the board of directors and that our board of directors will be divided into three classes, as nearly equal in number as possible, with the directors in each class serving for a three-year term, and one class being elected each year by our stockholders.

When considering whether directors have the experience, qualifications, attributes or skills, taken as a whole, to enable our board of directors to satisfy its oversight responsibilities effectively in light of our business and structure, the board of directors focuses primarily on each person's background and experience as reflected in the information discussed in each of the directors' individual biographies set forth above. We believe that our directors provide an appropriate mix of experience and skills relevant to the size and nature of our business.

Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our current directors will be divided among the three classes as follows:

- the Class I directors will be Allan R. Will, Brian Dovey and William W. Bradley, and their terms will expire at the annual meeting of stockholders to be held in 2023;

- the Class II directors will be Amy W. Schulman, Ajay Royan and Clive Meanwell, M.B., Ch.B., M.D., and their terms will expire at the annual meeting of stockholders to be held in 2024; and

- the Class III directors will be Harith Rajagopalan, M.D., Ph.D., Kelly Barnes and Marc Elia, and their terms will expire at the annual meeting of stockholders to be held in 2025.

Director Independence

Our board of directors has determined that, of our directors, Kelly Barnes, William W. Bradley, Brian Dovey, Marc Elia, Clive Meanwell, M.B., Ch.B, M.D., Ajay Royan, Amy W. Schulman and Allan R. Will do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of the Nasdaq Stock Market LLC, or the Nasdaq rules.

Board Leadership Structure

Our board of directors is currently chaired by Allan R. Will. Our corporate governance guidelines provide that, if the chairman of the board is a member of management or does not otherwise qualify as independent, the independent directors of the board may elect a lead director. The lead director's responsibilities include, but are not limited to: presiding over all meetings of the board of directors at which the chairman is not present, including any executive sessions of the independent directors; approving board meeting schedules and agendas; and acting as the liaison between the independent directors and the chief executive officer and chairman of the board. Our corporate governance guidelines further provide the flexibility for our board of directors to modify our leadership structure in the future as it deems appropriate.

Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through committee reports about such risks.

Board Committees

Our board of directors has established three standing committees—audit, compensation and nominating and corporate governance—each of which operates under a charter that will be approved by our board of directors. Upon our listing on the Nasdaq Global Market, each committee's charter has been available under the Corporate Governance section of our website at *www.fractyl.com*. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Audit Committee

The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;

- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- coordinating our board of directors' oversight of our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- discussing our risk management policies;
- meeting independently with our internal auditing staff, if any, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

The members of our audit committee are Kelly Barnes, Brian Dovey and Marc Elia. Kelly Barnes serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable Nasdaq rules. Our board of directors has determined that Kelly Barnes, Brian Dovey and Marc Elia meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Our board of directors has determined that Kelly Barnes is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules.

Compensation Committee

The compensation committee's responsibilities include:

- reviewing and approving, or recommending for approval by the board of directors, the compensation of our Chief Executive Officer and our other executive officers;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis," to the extent required; and
- preparing the annual compensation committee report required by SEC rules, to the extent required.

The members of our compensation committee are Clive Meanwell, M.B., Ch.B., M.D., Ajay Royan and Allan R. Will. Clive Meanwell, M.B., Ch.B, M.D. serves as the chairperson of the committee. Our board of directors has determined that each of Clive Meanwell, M.B., Ch.B., M.D., Ajay Royan and Allan R. Will is independent under the applicable Nasdaq rules, including the Nasdaq rules specific to membership on the compensation committee, and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become board members;
- recommending to our board of directors the persons to be nominated for election as directors and to each board committee;
- developing and recommending to our board of directors corporate governance guidelines, and reviewing and recommending to our board of directors proposed changes to our corporate governance guidelines from time to time; and
- overseeing a periodic evaluation of our board of directors.

The members of our nominating and corporate governance committee are William W. Bradley and Amy W. Schulman. William W. Bradley serves as the chairperson of the committee. Our board of directors has determined that William W. Bradley and Amy W. Schulman are independent under the applicable Nasdaq rules.

Compensation Committee Interlocks and Insider Participation

During 2021, the members of our compensation committee were Ajay Royan, Allan R. Will and Clive Meanwell, M.B., Ch.B., M.D. Mr. Royan is affiliated with one of our principal stockholders, Mithril. See "Certain Relationships and Related Person Transactions" for additional information on the securities acquired by Mithril and related agreements such stockholder is party to with us. None of our executive officers currently serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or compensation committee. None of the members of our compensation committee has ever been employed by us. For a description of transactions between us and members of our compensation committee and affiliates of such members, please see the section of this prospectus titled "Certain Relationships and Related Person Transactions."

Code of Ethics and Code of Conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon our listing on the Nasdaq Global Market, our code of business conduct and ethics will be available under the Corporate Governance section of our website at *www.fractyl.com*. In addition, we intend to post on our website all disclosures that are required by law or the Nasdaq rules concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

EXECUTIVE AND DIRECTOR COMPENSATION

This section discusses the material components of the executive compensation program for our executive officers who are named in the 2021 Summary Compensation Table below. In 2021, our named executive officers and their positions were as follows:

- Harith Rajagopalan, M.D., Ph.D., Chief Executive Officer;
- Lisa A. Davidson, Chief Financial Officer; and
- Margaret Borys, our former Chief Commercial Officer.

Ms. Borys's employment with us terminated on December 31, 2021.

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the completion of this offering may differ materially from the currently planned programs summarized in this discussion.

2021 Summary Compensation Table

The following table sets forth information concerning the compensation of our named executive officers for the year ended December 31, 2021.

Name and Principal Position	Year	Salary ($)(1)	Option Awards ($)(2)	Non-Equity Incentive Plan Compensation ($)(3)	All Other Compensation ($)(4)	Total ($)
Harith Rajagopalan, M.D., Ph.D. Chief Executive Officer	2021	480,960	997,094	187,209	—	1,665,263
Lisa A. Davidson Chief Financial Officer	2021	363,583	611,739	78,562	—	1,053,884
Margaret Borys Former Chief Commercial Officer	2021	430,769	495,962	86,000	307,328	1,320,058

(1) The amount for Ms. Borys includes $30,769 in accrued vacation paid in cash upon her termination of employment.

(2) Amounts reflect the full grant-date fair value of option awards granted during 2021 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of option awards in Note 12 to the consolidated financial statements included in this prospectus. For Ms. Borys, the amount also includes the incremental fair value of the modifications made to stock options under a separation agreement. Please refer to "Executive Compensation Arrangements" below for additional information regarding the separation agreement.

(3) Amounts represent the performance bonus earned for 2021. Please refer to "Narrative to Summary Compensation Table—2021 Bonuses" below for additional information regarding our 2021 bonus program.

(4) Amount represents company paid commuting expenses as well as payments and benefits under a separation agreement with Ms. Borys. Please refer to "Executive Compensation Arrangements" below for additional information regarding the separation agreement.

Narrative to Summary Compensation Table

2021 Salaries

The named executive officers receive a base salary to compensate them for services rendered to our company. The base salary payable to each named executive officer is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. Effective July 2021,

Dr. Rajagopalan's annual base salary increased from $409,763 to $550,000 and Ms. Davidson's annual base salary increased from $329,534 to $396,600. Ms. Borys did not receive a salary increase in 2021. The 2021 annual base salaries for our named executive officers were:

Named Executive Officer	2021 Annual Base Salary ($)
Harith Rajagopalan, M.D., Ph.D.	550,000
Lisa A. Davidson	396,600
Margaret Borys	400,000

2021 Bonuses

We offer our named executive officers the opportunity to earn annual cash bonuses to compensate them for attaining short-term goals as approved by our board of directors. For 2021, bonuses were based on attaining corporate and individual goals. Corporate goals for 2021 related to successfully progressing research and development programs toward regulatory milestones and market readiness, while furthering financial strategies. Individual goals for 2021 related to a named executive officer's area of responsibility within the company. No specific weightings were assigned to the 2021 goals. Our Board of Directors approved a 2021 annual target bonus as a percent of base salary for each named executive officer as follows:

- Harith Rajagopalan, M.D., Ph.D.: 35%
- Lisa A. Davidson: 20%
- Margaret Borys: 20%

The actual amount of these bonuses is set forth in the "Non-Equity Incentive Plan Compensation" column of the 2021 Summary Compensation Table above.

Equity Compensation

We have historically granted stock options to our employees, including our named executive officers, as the long-term incentive component of our compensation program. Our stock options generally allow employees to purchase shares of our common stock at a price equal to the fair market value of our common stock on the date of grant, as determined by our board of directors. Stock option grants made to new hires typically vest as to 25% of the underlying shares on the first anniversary of the employment commencement date and in equal monthly installments over the following three years. Stock option grants made to existing employees typically vest in 48 equal monthly installments following the date of grant. Historically, our stock options have been intended to qualify as "incentive stock options" to the extent permitted under the Internal Revenue Code.

The following table sets forth the options granted to our named executive officers during 2021 under our 2011 Stock Incentive Plan, as amended and restated, which we refer to as the 2011 Plan. These stock options have exercise prices equal to the fair market value of our common stock on the date of grant, as determined by the board of directors, and are subject to our standard vesting schedule for existing employees described above.

Named Executive Officer	2021 Options Granted
Harith Rajagopalan, M.D., Ph.D.	564,265
Lisa A. Davidson	345,982
Margaret Borys	273,090

Prior to this offering, we intend to adopt a 2022 Incentive Award Plan, referred to below as the 2022 Plan, in order to facilitate the grant of cash and equity incentives to directors, employees (including our named

executive officers) and consultants of the Company and certain of its affiliates to enable the Company and certain of its affiliates to obtain and retain services of these individuals, which we consider to be essential to our long-term success. Following the effective date of the 2022 Plan, we will cease making any further grants under the 2011 Plan. However, the 2011 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. For additional information about the 2022 Plan, please see the section titled "Incentive Compensation Plans—2022 Incentive Award Plan" below.

Other Elements of Compensation

Retirement Plan. We currently maintain a 401(k) retirement savings plan for our employees who satisfy certain eligibility requirements. Our named executive officers are eligible to participate in the 401(k) plan on the same terms as other full-time employees. The Internal Revenue Code allows eligible employees to defer a portion of their compensation, within prescribed limits, on a pre-tax basis through contributions to the 401(k) plan. We believe that providing a vehicle for tax-deferred retirement savings though our 401(k) plan adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our named executive officers, in accordance with our compensation policies. For 2021, we did not make employer contribution to the 401(k) plan.

Health and Welfare Plans. Our named executive officers are eligible to participate in our health and welfare plans, including medical, dental and vision benefits, medical and dependent care flexible spending accounts, short-term and long-term disability insurance and life insurance and accidental death & dismemberment insurance, on the same terms as our other full time employees.

Executive Compensation Arrangements

Prior to this offering, we intend to enter into employment agreements with Dr. Rajagopalan and Ms. Davidson that will supersede their prior agreements with us. The material terms of these agreements will be described in this prospectus once they are finalized.

Separation Agreement with Margaret Borys

In connection with her termination of employment, we entered into a separation agreement with Ms. Borys, effective as of January 18, 2022, which provides for her to receive, in consideration for her execution and non-revocation of a waiver and release of claims, (1) a lump sum payment of $233,334, (2) payment of COBRA continuation coverage premiums for up to seven months, (3) payment of her unpaid fiscal year 2021 cash bonus, based on achievement of applicable performance criteria, (4) an extension of the exercise period on Ms. Borys's vested stock options to December 31, 2022 and (5) a housing stipend equal to $9,000 plus a gross-up for associated taxes.

Outstanding Equity Awards at 2021 Fiscal Year-End

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each named executive officer as of December 31, 2021.

		Option Awards			
Name	Vesting Start Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)	Option Exercise Price ($)	Option Expiration Date
Harith Rajagopalan, M.D., Ph.D.	—	502,069	—	0.38	10/15/2023
	—	409,820	—	0.79	11/10/2024
	—	265,000	—	0.79	2/9/2025
	—	740,538	—	1.24	12/16/2025
	—	386,000	—	1.24	6/26/2026
	—	906,634	—	1.56	3/13/2028

		Option Awards			
Name	Vesting Start Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)	Option Exercise Price ($)	Option Expiration Date
	3/26/2020	445,986	573,412	1.81	3/25/2030
	6/24/2021	70,533	493,732	3.25	6/23/2031
Lisa A. Davidson	—	516,076	—	1.24	12/16/2025
	1/1/2019	83,612	31,056	1.55	3/26/2029
	9/25/2019	25,570	19,888	1.81	9/24/2029
	3/26/2020	93,721	120,499	1.81	3/25/2030
	6/24/2021	43,247	302,735	3.25	6/23/2031
Margaret Borys	—	677,719	—	1.55	12/18/2028
	—	43,863	—	1.81	3/25/2030
	—	34,136	—	3.25	6/23/2031

(1) The options vest in 48 equal monthly installments following the vesting start date.

Director Compensation

None of our directors other than Dr. Rajagopalan received compensation from us during 2021. Dr. Rajagopalan's compensation from us for 2021 is disclosed in the 2021 Summary Compensation Table and related narrative disclosure.

The table below shows the aggregate numbers of option awards (exercisable and unexercisable) and unvested stock awards held as of December 31, 2021 by each of our non-employee directors who was serving as of December 31, 2021.

Name	Options Award (#)	Stock Awards (#)
William W. Bradley	863,988(1)	—
Brian Dovey	—	—
Marc Elia	—	—
Michael L. Huang	—	—
Clive Meanwell	—	—
Ajay Royan	—	—
Amy W. Schulman	267,127	—
Allan R. Will	890,422	—

(1) Includes 400,000 options that Mr. Bradley transferred to the Hillcrest Irrevocable Trust.

Effective upon this offering, we intend to approve and implement a compensation program for our non-employee directors that consists of annual retainer fees and long-term equity awards. The material terms of this program will be described in this prospectus once they are finalized.

Incentive Compensation Plans

The following summarizes the material terms of the 2022 Incentive Award Plan, or the 2022 Plan, the 2022 Employee Stock Purchase Plan, or the ESPP, which will be the long-term incentive compensation plans in which our directors and named executive officers are eligible to participate following the consummation of this offering, and the 2011 Plan, under which we have previously made periodic grants of equity and equity-based awards to our directors and named executive officers.

2022 Incentive Award Plan

Effective the day prior to the first public trading date of our common stock, we intend to adopt and ask our stockholders to approve the 2022 Plan, under which we may grant cash and equity-based incentive awards to

eligible service providers in order to attract, retain and motivate the persons who make important contributions to our company. The material terms of the 2022 Plan are summarized below.

Eligibility and Administration

Our employees, consultants and directors, and employees and consultants of our subsidiaries, will be eligible to receive awards under the 2022 Plan. The 2022 Plan will be administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations imposed under the 2022 Plan, Section 16 of the Exchange Act, stock exchange rules and other applicable laws. The plan administrator will have the authority to take all actions and make all determinations under the 2022 Plan, to interpret the 2022 Plan and award agreements and to adopt, amend and repeal rules for the administration of the 2022 Plan as it deems advisable. The plan administrator will also have the authority to grant awards, determine which eligible service providers receive awards and set the terms and conditions of all awards under the 2022 Plan, including any vesting and vesting acceleration provisions, subject to the conditions and limitations in the 2022 Plan.

Shares Available for Awards

An aggregate of shares of our common stock will initially be available for issuance under the 2022 Plan. The number of shares initially available for issuance will automatically increase on January 1 of each calendar year beginning in 2023 and ending in and including 2032, equal to the lesser of (A) % of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (B) a smaller number of shares determined by our board of directors. No more than shares of common stock may be issued under the 2022 Plan upon the exercise of incentive stock options. Shares issued under the 2022 Plan may be authorized but unissued shares, shares purchased on the open market or treasury shares.

If an award under the 2022 Plan or the 2011 Plan, expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the 2022 Plan. Awards granted under the 2022 Plan in substitution for any options or other stock or stock-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the 2022 Plan, but may count against the maximum number of shares that may be issued upon the exercise of incentive stock options, or ISOs.

Awards

The 2022 Plan provides for the grant of ISOs, nonqualified stock options, or NSOs, stock appreciation rights, or SARs, restricted stock, dividend equivalents, restricted stock units, or RSUs, and other stock or cash-based awards. Certain awards under the 2022 Plan may constitute or provide for payment of "nonqualified deferred compensation" under Section 409A of the Code. All awards under the 2022 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows:

- *Stock Options and SARs*. Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Code are satisfied. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR. The exercise price of a stock option or SAR will not be less than 100% of the fair market value of the underlying share on the grant date

(or 110% in the case of ISOs granted to certain significant stockholders), except with respect to certain substitute awards granted in connection with a corporate transaction. The term of a stock option or SAR may not be longer than ten years (or five years in the case of ISOs granted to certain significant stockholders).

- *Restricted Stock and RSUs*. Restricted stock is an award of nontransferable shares of our common stock that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver shares of our common stock in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on shares of our common stock prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted stock and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the 2022 Plan.

- *Other Stock or Cash Based Awards*. Other stock or cash-based awards are awards of cash, fully vested shares of our common stock and other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock or other property. Other stock or cash-based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other stock or cash-based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

Performance Criteria

The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under the 2022 Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on stockholders' equity; total stockholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately

be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

Certain Transactions

In connection with certain corporate transactions and events affecting our common stock, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2022 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the 2022 Plan and replacing or terminating awards under the 2022 Plan. In addition, in the event of certain non-reciprocal transactions with our stockholders, the plan administrator will make equitable adjustments to awards outstanding under the 2022 Plan as it deems appropriate to reflect the transaction.

Provisions of the 2022 Plan Relating to Director Compensation

The 2022 Plan provides that the plan administrator may establish compensation for non-employee directors from time to time subject to the 2022 Plan's limitations. Prior to commencing this offering, we intend to approve and implement a compensation program for our non-employee directors, which is described above under the heading "Director Compensation." Our board of directors (or its authorized committee) may modify the non-employee director compensation program from time to time in the exercise of its business judgment, taking into account such factors, circumstances and considerations as it shall deem relevant from time to time, provided that the sum of any cash compensation or other compensation and the grant date fair value of any equity awards granted under the 2022 Plan as compensation for services as a non-employee director during any fiscal year may not exceed $ in the fiscal year of the non-employee director's initial service and $ in any other fiscal year. The plan administrator may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the plan administrator may determine in its discretion, subject to the limitations in the 2022 Plan.

Plan Amendment and Termination

Our board of directors may amend or terminate the 2022 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2022 Plan, may materially and adversely affect an award outstanding under the 2022 Plan without the consent of the affected participant and stockholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator may, without the approval of our stockholders, amend any outstanding stock option or SAR to reduce its price per share, other than in the context of corporate transactions or equity restructurings, as described above. The 2022 Plan will remain in effect until the tenth anniversary of its effective date, unless earlier terminated by our board of directors. No awards may be granted under the 2022 Plan after its termination.

Foreign Participants, Claw-Back Provisions, Transferability and Participant Payments

The plan administrator may modify awards granted to participants who are foreign nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under the 2022 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a

domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2022 Plan and exercise price obligations arising in connection with the exercise of stock options under the 2022 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or check, shares of our common stock that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

2022 Employee Stock Purchase Plan

Effective the day prior to the first public trading date of our common stock, we intend to adopt and ask our stockholders to approve the ESPP, the material terms of which are summarized below.

Shares Available for Awards; Administration

A total of shares of our common stock will initially be reserved for issuance under the ESPP. In addition, the number of shares available for issuance under the ESPP will be annually increased on January 1 of each calendar year beginning in 2023 and ending in and including 2032, by an amount equal to the lesser of (A) % of the shares outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares as is determined by our board of directors, provided that no more than shares of our common stock may be issued under the ESPP. Our board of directors or a committee of our board of directors will administer and will have authority to interpret the terms of the ESPP and determine eligibility of participants. We expect that the compensation committee will be the initial administrator of the ESPP.

Eligibility

All of our employees are eligible to participate in the ESPP, unless the administrator determines to limit participation in accordance with the terms of the ESPP and provided that an employee may not be granted rights to purchase stock under our ESPP if the employee, immediately after the grant, would own (directly or through attribution) stock possessing 5% or more of the total combined voting power or value of all classes of our stock.

Grant of Rights

The ESPP is intended to qualify under Section 423 of the Code and stock will be offered under the ESPP during offering periods. The length of the offering periods under the ESPP will be determined by the plan administrator and may be up to twenty-seven months long. Employee payroll deductions will be used to purchase shares on each purchase date during an offering period. The purchase dates for each offering period will be the final trading day in the offering period. Offering periods under the ESPP will commence when determined by the plan administrator. The plan administrator may, in its discretion, modify the terms of future offering periods.

The ESPP permits participants to purchase common stock through payroll deductions of up to a specified percentage of their eligible compensation. The plan administrator will establish a maximum number of shares that may be purchased by a participant during any offering period. In addition, no employee will be permitted to accrue the right to purchase stock under the ESPP at a rate in excess of $25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our common stock as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase shares of our common stock. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the purchase date. Participants may voluntarily end their participation in the ESPP at any time during a specified period prior to the end of the

applicable offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer options granted under the ESPP other than by will or the laws of descent and distribution, and options granted under the ESPP are generally exercisable only by the participant.

Certain Transactions

In the event of certain non-reciprocal transactions or events affecting our common stock, the plan administrator will make equitable adjustments to the ESPP and outstanding rights. In the event of certain unusual or non-recurring events or transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares of stock subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase stock on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights.

Plan Amendment

The plan administrator may amend, suspend or terminate the ESPP at any time. However, stockholder approval will be obtained for any amendment that increases the aggregate number or changes the type of shares that may be sold pursuant to rights under the ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in the ESPP or changes the ESPP in any manner that would cause the ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Code.

2011 Stock Incentive Plan

Our board of directors and stockholders have approved the 2011 Plan, under which we may grant stock options and other stock-based awards to employees, directors and consultants of our company or its affiliates. We have reserved a total of shares of our common stock for issuance under the 2011 Plan.

Following the effectiveness of the 2022 Plan, we will not make any further grants under the 2011 Plan. However, the 2011 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. As discussed above, we anticipate that shares of our common stock subject to awards granted under the 2011 Plan that are forfeited, lapse unexercised or are settled in cash will again be available for issuance under the 2022 Plan.

Eligibility and Administration

Our employees, officers, directors, consultants and advisors are eligible to be granted awards under the 2011 Plan. Our board of directors administers the 2011 Plan and has the authority to determine recipients of awards and the terms of awards granted under the 2011 Plan, to interpret the 2011 Plan and awards outstanding thereunder, and to make changes to awards outstanding under the 2011 Plan, provided that such changes may not impair a participant's rights under the plan without the participant's consent. The board of directors may delegate its authority under the 2011 Plan to a committee.

Types of Awards

The 2011 Plan provides for the grant of non-qualified and incentive stock options, restricted stock, restricted stock units and other stock-based awards to eligible participants. As of the date of this prospectus, awards of stock options are outstanding under the 2011 Plan.

Certain Transactions

If certain changes are made in, or events occur with respect to, our common stock, the 2011 Plan and outstanding awards will be appropriately adjusted in the class, number and, as applicable, exercise price of securities as determined by the plan administrator. In the event of certain corporate transactions of our company, including a consolidation, merger, or a liquidation, our board of directors may make appropriate provision for the assumption or equitable substitution of outstanding awards, provide for the assumption or replacement of outstanding stock options, terminate awards for a cash payment equal to the excess of the fair market value of the underlying shares over the exercise or purchase price of the applicable award or provide that all stock options will terminate if not exercised within a specified number of days. The vesting and exercisability of awards may accelerate in connection with such a transaction, either by action of the plan administrator or under the terms of the applicable award agreements.

Amendment and Termination

The plan administrator may amend, suspend or terminated the 2011 Plan or any portion thereof from time to time, provided that the board of directors determines that any amendment does not materially and adversely affect the rights of participants under the 2011 Plan. Any amendment the plan administrator determines requires stockholder approval under the Internal Revenue Code will be subject to approval by our stockholders. The 2011 Plan will terminate on ten years from the earlier of date of its adoption by the board of directors or its approval by our stockholders, if not earlier terminated by the board of directors.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following includes a summary of transactions since January 1, 2019 to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock, or 5% Security Holders, or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive and Director Compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

Related Party Agreements in Effect Prior to this Offering

Series E Preferred Stock

From March to July 2020, we issued and sold to investors in a private placement an aggregate of 12,729,465 shares of Series E Preferred Stock at a purchase price of $4.2893 per share, for aggregate consideration of approximately $54.6 million.

The following table sets forth the aggregate number of Series E Preferred Stock acquired by 5% Security Holders in the financing transactions described above.

Participants(1)	Series E Preferred Stock	Aggregate Purchase Price (in thousands)
Entities affiliated with Mithril(2)	373,021	$ 1,600
Entities affiliated with General Catalyst(3)	233,138	$ 1,000
Entities affiliated with Bessemer Venture Partners(4)	352,159	$ 1,511
Entities affiliated with Domain Associates, L.L.C.(5)	349,707	$ 1,500
CVF, LLC	2,914,228	$ 12,500

(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the caption "Principal Stockholders."

(2) Consists of 373,021 shares of Series E Preferred Stock purchased by Mithril II LP. Ajay Royan, one of our directors, is the Managing General Partner and Founder of Mithril Capital Management LLC, or MCM. MCM is a management company that manages Mithril II LP and is appointed by Mithril II GP LP, the general partner of Mithril II LP.

(3) Consists of 228,371 shares of Series E Preferred Stock purchased by General Catalyst Group V, L.P., or GCGV, and 4,767 shares of Series E Preferred Stock purchased by GC Entrepreneurs Fund V, L.P, or GCEV.

(4) Consists of 112,691 shares of Series E Preferred Stock purchased by Bessemer Venture Partners VII L.P., 49,302 shares of Series E Preferred Stock purchased by Bessemer Venture Partners VII Institutional L.P. and 190,166 shares of Series E Preferred Stock purchased by BVP VII Special Opportunity Fund L.P.

(5) Consists of 347,131 shares of Series E Preferred Stock purchased by Domain Partners VIII, L.P. and 2,576 shares of Series E Preferred Stock purchased by DP VIII Associates, L.P. Brian Dovey, one of our directors, is a partner of Domain Associates, L.L.C.

Series F Preferred Stock

In June and July 2021, we issued and sold to investors in a private placement an aggregate of 11,927,048 shares of Series F Preferred Stock at a purchase price of $8.3843 per share, for aggregate consideration of approximately $100.0 million.

The following table sets forth the aggregate number of Series F Preferred Stock acquired by 5% Security Holders in the financing transactions described above.

Participants(1)	Series F Preferred Stock	Aggregate Purchase Price (in thousands)
Entities affiliated with Mithril(2)	1,598,225	$ 13,400
CVF, LLC	333,957	$ 2,800
Entities affiliated with Marc Elia(3)	2,981,763	$ 25,000
Entities affiliated with Clive Meanwell, M.B., Ch.B, M.D.(4)	596,352	$ 5,000

(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the caption "Principal Stockholders."

(2) Consists of 1,598,225 shares of Series F Preferred Stock purchased by Mithril II LP. Ajay Royan, one of our directors, is the Managing General Partner and Founder of MCM. MCM is a management company that manages Mithril II LP and is appointed by Mithril II GP LP, the general partner of Mithril II LP.

(3) Consists of 954,164 shares of Series F Preferred Stock purchased by Sparviero LP and 2,027,599 shares of Series F Preferred Stock purchased by M28 Capital Master Fund LP.

(4) Consists of 596,352 shares of Series F Preferred Stock purchased by Population Health Capital Partners II, L.P.

Convertible Note

In January 2022, we sold and issued approximately $20.1 million aggregate principal amount of convertible promissory notes, or the 2022 Notes, in a private placement transaction. Maverick Designated Investments Fund, L.P. purchased $5.0 million of the 2022 Notes, Maverick Growth Fund, L.P. purchased $5.0 million of the 2022 Notes, ECWC Holdings LLC purchased $10.0 million of the 2022 Notes and Jordan Rubin purchased approximately $0.1 million of the 2022 Notes.

Immediately prior to the completion of this offering, the 2022 Notes will be converted into a number of shares of common stock determined at a conversion price equal to the lesser of (i) 80% of the price per share of the shares offered hereby or (ii) a price per share equal to $1.1 billion divided by our fully diluted capitalization as of immediately prior to the closing of this offering.

Amended and Restated Investors' Rights Agreement

In connection with the issuance of our Series F Preferred Stock in June and July 2021, we entered into a Fifth Amended and Restated Investors' Rights Agreement, or the IRA, with certain holders of our preferred stock, many which are beneficial holders of more than 5% of our capital stock or are entities with which certain of our directors are affiliated. The IRA imposes certain affirmative obligations on us and also grants certain rights to holders, including certain registration rights with respect to the securities held by them, certain information and observer rights, and certain additional rights. Certain provisions of the IRA will terminate in connection with this offering. See "Description of Capital Stock—Registration Rights" for additional information.

Amended and Restated Voting Agreement

We are a party to an amended and restated voting agreement with certain of our stockholders, pursuant to which each of our directors was elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve. Our voting agreement will terminate by its terms in connection with the closing of this offering, and members previously elected to our board of directors pursuant to this voting agreement will continue to serve as directors until they resign, are removed or their successors are duly elected by the holders of our common stock. The composition of our board of directors after this offering is described in more detail under "Management—Composition of our Board of Directors.

The Voting Agreement, including its provisions concerning the rights of certain of the holders to designate directors, will automatically terminate upon the consummation of this offering.

Amended and Restated Right of First Refusal and Co-Sale Agreement

In connection with the issuance of our Series F Preferred Stock in June and July 2021, we entered into a Fifth Amended and Restated Right of First Refusal and Co-Sale Agreement, or the ROFR and Co-Sale Agreement, with certain of our preferred stockholders, many of which are beneficial holders of more than 5% of our capital stock or are entities with which certain of our directors are affiliated. The ROFR and Co-Sale Agreement, among other things: (a) grants our investors certain rights of first refusal and co-sale with respect to proposed transfers of our securities by certain preferred stockholders; and (b) grants us certain rights of first refusal with respect to proposed transfers of our securities by certain preferred stockholders.

The ROFR and Co-Sale Agreement will automatically terminate immediately prior to the completion of this offering.

Employment Agreements

We have entered into employment agreements or consulting agreements with certain of our executive officers. See "Executive and Director Compensation—Executive Compensation Arrangements."

Director and Officer Indemnification and Insurance

Prior to the consummation of this offering, we intend to enter into separate indemnification agreements with each of our directors and executive officers. We have also purchased directors' and officers' liability insurance. See "Description of Capital Stock—Limitations on Liability and Indemnification of Officers and Directors."

Policies and Procedures for Related Person Transactions

Our board of directors has adopted a written related person transaction policy, to be effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds $120,000 in any fiscal year and a related person had, has or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

PRINCIPAL STOCKHOLDERS

The following table sets forth information as of March 31, 2022 with respect to the beneficial ownership of our common stock by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The number of shares beneficially owned by each stockholder is determined in accordance with the rules issued by the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power, which includes the power to dispose of or to direct the disposition of such security. Except as indicated in the footnotes below, we believe, based on the information furnished to us, that the individuals and entities named in the table below have sole voting and investment power with respect to all shares of common stock beneficially owned by them, subject to any community property laws.

Percentage ownership of our common stock before this offering is based on shares of common stock outstanding as of March 31, 2022. Percentage ownership of our common stock after this offering is based on shares of common stock as of March 31, 2022, after giving effect to our issuance of shares of our common stock in this offering. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options, warrants or other rights held by such person that are currently exercisable or will become exercisable within 60 days of March 31, 2022 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed stockholders is c/o Fractyl Health, Inc., 17 Hartwell Avenue Lexington, Massachusetts 02421.

	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
Name of Beneficial Owner	Number	Percentage	Number	Percentage
5% or Greater Stockholders				
Entities affiliated with Mithril(1)				
Entities affiliated with General Catalyst(2)				
Entities affiliated with Bessemer Venture Partners(3)				
Entities affiliated with Domain Associates, L.L.C.(4)				
CVF, LLC(5)				
Named Executive Officers and Directors				
Harith Rajagopalan, M.D., Ph.D.(6)				
Lisa A. Davidson(7)				
Margaret Borys(8)				
Kelly Barnes				
William W. Bradley(9)				
Brian Dovey(4)				
Entities affiliated with Marc Elia(10)				
Entities affiliated with Clive Meanwell, M.B., Ch.B., M.D.(11)				
Ajay Royan(1)				
Amy W. Schulman(12)				

Name of Beneficial Owner	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
	Number	Percentage	Number	Percentage
Allan R. Will(13)				
All current executive officers and directors as a group (12 persons)(14)				

* Represents beneficial ownership of less than 1%.

(1) Consists of (a) shares of common stock issuable upon conversion of Series C-1 Preferred Stock purchased by Mithril LP, (b) shares of common stock issuable upon conversion of Series C-2 Preferred Stock purchased by Mithril LP, (c) shares of common stock issuable upon conversion of Series D Preferred Stock purchased by Mithril LP, (d) shares of common stock issuable upon conversion of Series E Preferred Stock purchased by Mithril II LP and (e) shares of common stock issuable upon conversion of Series F Preferred Stock purchased by Mithril II LP. Mr. Royan is the Managing General Partner and Founder of MCM. MCM is a management company that manages each of Mithril LP and Mithril II LP. Mr. Royan and Peter Thiel are the members of the investment committee of Mithril GP LP, the general partner of Mithril LP and the members of the investment committee established by Mithril II GP LP, the general partner of Mithril II LP. Each of the investment committees makes all investment decisions with respect to shares held by each of Mithril LP and Mithril II LP, respectively, and may be deemed to have shared voting, investment and dispositive power with respect to the securities held by each of Mithril LP and Mithril II LP.

(2) Consists of (i) shares of common stock held of record by General Catalyst Group V, L.P., or GCGV, (ii) shares of common stock held of record by GC Entrepreneurs Fund V, L.P., or GCEV, (iii) shares of common stock issuable upon conversion of convertible preferred stock purchased by GCGV, and (iv) shares of common stock issuable upon conversion of convertible preferred stock purchased by GCEV.

General Catalyst GP V, LLC, or GCGPV, is the general partner of General Catalyst Partners V, L.P., which is the general partner of GCGV and GCEV.

Joel Cutler, David Fialkow and Hemant Taneja are managing directors of GCGPV, and, as a result, may be deemed to share voting and investment power with respect to the shares held by GCGV and GCEV.

Each party named above disclaims beneficial ownership of such shares. The principal business address of the foregoing entities and persons is 20 University Road, Suite 450, Cambridge, MA 02138.

(3) Consists of (i) shares of common stock issuable upon he deemed conversion of shares of the convertible preferred stock held of record by Bessemer Venture Partners VII L.P. (BVP VII), (ii) shares of common stock issuable upon the deemed conversion of shares of the convertible preferred stock held of record by Bessemer Venture Partners VII Institutional L.P. (BVP VII Institutional) and (iii) shares of common stock issuable upon the deemed conversion of shares of the convertible preferred stock held of record by BVP VII Special Opportunity Fund L.P. (BVP SOF, and together with BVP VII and BVP VII Institutional, the BVP Entities). Deer VII & Co. L.P. (Deer VII L.P.) is the general partner of the BVP Entities. Deer VII & Co. Ltd. (Deer VII Ltd.) is the general partner of Deer VII L.P. Robert P. Goodman, David Cowan, Jeremy Levine, Byron Deeter and Robert M. Stavis are the directors of Deer VII Ltd. and hold the voting and dispositive power for the BVP Entities. Investment and voting decisions with respect to the shares held by the BVP Entities are made by the directors of Deer VII Ltd. acting as an investment committee. The address of each of these entities is c/o Bessemer Venture Partners, 1865 Palmer Ave., Suite 104, Larchmont, NY 10538.

(4) Consists of shares of common stock issuable upon conversion of convertible preferred stock held by Domain Partners VIII, L.P. (Domain VIII) and shares of common stock issuable upon conversion of convertible preferred stock held by DP VIII Associates, L.P. (DP VIII). Brian H. Dovey, a member of our Board of Directors, is a managing member of One Palmer Square Associates VIII, L.L.C., the General

Partner of Domain VIII and DP VIII. The managing members of One Palmer Square Associates VIII, L.L.C. share voting and investment power with respect to shares beneficially owned by Domain VIII and DP VIII. Mr. Dovey disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of Domain VIII and DP VIII is 103 Carnegie Center, Suite 300, Princeton, NJ 08540.

(5) Consists of shares of common stock issuable upon conversion of convertible preferred stock held by CVF, LLC. Richard H. Robb, manager of CVF, LLC, exercises voting and investment power with respect to the shares held by CVF, LLC. The address of CVF, LLC is 222 N. LaSalle Street, Suite 2000, Chicago, IL 60601.

(6) Consists of (i) shares of common stock and common stock issuable upon conversion of convertible preferred stock, (ii) shares of common stock and common stock issuable upon conversion of convertible preferred stock held by various family trusts for which Harith Rajagopalan serves as the Investment Advisor and, as a result, exercises voting and dispositive power with respect to such shares, and (iii) shares of common stock underlying options exercisable within 60 days from March 31, 2022.

(7) Consists of (i) shares of common stock and (ii) shares of common stock underlying options exercisable within 60 days from March 31, 2022.

(8) Consists of shares of common stock underlying options exercisable within 60 days from March 31, 2022.

(9) Consists of shares of common stock underlying options exercisable within 60 days from March 31, 2022.

(10) Consists of shares of common stock issuable upon conversion of Series F Preferred Stock held by M28 Capital Master Fund LP, or M28 Capital, and shares of common stock issuable upon conversion of Series F Preferred Stock held by Sparviero LP. Marc Elia, a member of our Board of Directors, is a managing member of M28 Capital Fund GP LLC, the general partner of M28 Capital and Sparviero LP, and, as a result, may be deemed to share voting and investment power with respect to the shares held by each. Mr. Elia disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of M28 Capital and Sparviero LP is 700 Canal Street, 2nd Floor, Stamford, Connecticut 06902.

(11) Consists of shares of common stock issuable upon conversion of Series F Preferred Stock held by Population Health Capital Partners II, L.P., or PHPII. Clive Meanwell, M.B., Ch.B., M.D., a member of our Board of Directors, is the Founder of Population Health Partners GP, LLC, the general partner of PHPII, and, as a result, may be deemed to share voting and investment power with respect to the shares held by PHPII. Dr. Meanwell disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of PHPII is 50 Mountaintop Road, Bernardsville, New Jersey 07924.

(12) Consists of shares of common stock underlying options exercisable within 60 days from March 31, 2022.

(13) Consists of shares of common stock underlying options exercisable within 60 days from March 31, 2022.

(14) Consists of (i) shares of common stock, (ii) shares of common stock issuable upon conversion of convertible preferred stock, and (iii) shares of common stock underlying options exercisable within 60 days from March 31, 2022.

DESCRIPTION OF CAPITAL STOCK

Capital Structure

The following description of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will be in effect upon the closing of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of our common stock and preferred stock reflect changes to our capital structure that will occur upon the closing of this offering.

As of March 31, 2022, shares of our common stock were outstanding and held by stockholders of record. This amount assumes the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock, which will occur immediately prior to the closing of this offering. Additionally, in connection with the closing of this offering, the 2022 Notes will automatically settle into shares of our common stock, assuming an initial public offering price per share of $, which is the midpoint of the price range set forth on the cover page of this prospectus.

General

At or prior to the consummation of this offering, we will file an amended and restated certificate of incorporation and we will adopt our amended and restated bylaws. Our amended and restated certificate of incorporation will authorize capital stock consisting of:

- shares of common stock, par value $0.00001 per share; and
- shares of preferred stock, par value $0.00001 per share.

We are selling shares of common stock in this offering (shares if the underwriters exercise their option to purchase additional shares of our common stock in full). All shares of our common stock outstanding upon consummation of this offering will be fully paid and non-assessable.

The following summary describes the material provisions of our capital stock. We urge you to read our amended and restated certificate of incorporation and our amended and restated bylaws, which are included as exhibits to the registration statement of which this prospectus forms a part.

Certain provisions of our amended and restated certificate of incorporation and our amended and restated bylaws summarized below may be deemed to have an anti-takeover effect and may delay or prevent a tender offer or takeover attempt that a stockholder might consider in its best interest, including those attempts that might result in a premium over the market price for the shares of common stock.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Upon our dissolution or liquidation, after payment in full of all amounts required to be paid to creditors and to the holders of preferred stock having liquidation preferences, if any, the holders of shares of our common stock will be entitled to receive pro rata our remaining assets available for distribution for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding.

Preferred Stock

Upon the closing of this offering, (i) all outstanding shares of our convertible preferred stock will be converted into shares of our common stock, and (ii) all outstanding shares of our convertible preferred stock will be cancelled.

Upon the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of March 31, 2022, options to purchase shares of our common stock were outstanding under our 2011 Plan, of which options were vested of that date.

Registration Rights

Under the IRA, following the consummation of this offering, certain holders of our common stock will be entitled to certain rights with respect to the registration of such shares for public resale under the Securities Act, until the rights otherwise terminate pursuant to the terms of the IRA. Pursuant to the IRA, beginning six months after the completion of this offering, the holders of up to shares of our common stock, or certain transferees, will be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Form S-1 Registration Rights

Pursuant to the IRA, certain holders of common stock are entitled to certain demand registration rights, including to demand registration of their registrable securities on a registration statement on Form S-1 at any time after 180 days following the completion of this offering. The holders of at least 30% of the registrable securities have the right to require us to file a registration statement on Form S-1 under the Securities Act in order to register the resale of their shares of common stock; *provided*, that no such registration is required to be made (i) during the period that is 60 days before our good faith estimate of the date of filing of, and ending on a date that is 180 days after the effective date of, a Company-initiated registration, (ii) at such time as we have effected two such registration statements, or (iii) if the holders who initiated the registration request propose to dispose of shares of registrable securities that may be immediately registered on Form S-3 pursuant to a request under the IRA. We may, in certain circumstances, defer such registrations, and the underwriters have the right, subject to certain limitations, to limit the number of shares included in such registrations.

Piggyback Registration Rights

If at any time after this offering we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 Registration

After we are qualified for registration on Form S-3, the holders, as holders of registrable securities, may make a written request that we register the offer and sale of their shares on a Form S-3 registration statement, having an anticipated aggregate offering price of at least $2,000,000; provided, that no such registration is required to be made (i) during the period that is 30 days before our good faith estimate of the date of filing of, and ending on a date that is 90 days after the effective date of, a Company-initiated registration, or (ii) at such time as we have effected two such registrations within the 12-month period immediately preceding the date of such request. We may, in certain circumstances, defer such registrations, and the underwriters have the right, subject to certain limitations, to limit the number of shares included in such registrations.

Expenses and Indemnification

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration, filing and qualification fees; printers' and accounting fees; fees and disbursements of our counsel; and reasonable fees and disbursements of a counsel for the selling securityholders. Additionally, we have agreed to indemnify selling stockholders for damages, and any legal or other expenses reasonably incurred, arising from or based upon any untrue statement of a material fact contained in any registration statement, an omission or alleged omission to state a material fact in any registration statement or necessary to make the statements therein not misleading, or any violation or alleged violation by the indemnifying party of securities laws, subject to certain exceptions.

Termination of Registration Rights

The registration rights terminate as to any shares of registrable securities upon the earliest of: (i) such shares have been registered under the Securities Act pursuant to an effective registration statement filed thereunder and disposed of in accordance with the registration statement covering them, (ii) such shares may be publicly sold pursuant to Rule 144 of the Securities Act, (iii) the fifth anniversary of the completion of this offering, or (iv) the closing of a deemed liquidation event.

Choice of Forum

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers or stockholders to us or to our stockholders; (iii) any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws (as either may be amended from time to time); and (iv) any action asserting a claim against us that is governed by the internal affairs doctrine. As a result, any action brought by any of our stockholders with regard to any of these matters will need to be filed in the Court of Chancery of the State of Delaware and cannot be filed in any other jurisdiction; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of

Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws will also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause or causes of action against us or any defendant arising under the Securities Act. Such provision is intended to benefit and may be enforced by us, our officers and directors, employees and agents, including the underwriters and any other professional or entity who has prepared or certified any part of this prospectus. Nothing in our amended and restated certificate of incorporation and amended and restated bylaws preclude stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

If any action the subject matter of which is within the scope described above is filed in a court other than a court located within the State of Delaware, or a Foreign Action, in the name of any stockholder, such stockholder shall be deemed to have consented to the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to enforce the applicable provisions of our amended and restated certificate of incorporation and amended and restated bylaws and having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the Foreign Action as agent for such stockholder. Although our amended and restated certificate of incorporation and amended and restated bylaws will contain the choice of forum provision described above, it is possible that a court could find that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims or make such lawsuits more costly for stockholders, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder.

Dividends

Declaration and payment of any dividend will be subject to the discretion of our board of directors. The time and amount of dividends will be dependent upon our business prospects, results of operations, financial condition, cash requirements and availability, debt repayment obligations, capital expenditure needs, contractual restrictions, covenants in the agreements governing our current and future indebtedness, industry trends, the provisions of Delaware law affecting the payment of distributions to stockholders and any other factors our board of directors may consider relevant. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business and to repay indebtedness, and therefore do not anticipate declaring or paying any cash dividends on our common stock in the foreseeable future. See "Dividend Policy" and "Risk Factors—Risks Related to this Offering and Ownership of our Common Stock— We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock."

Anti-Takeover Provisions

Our amended and restated certificate of incorporation and amended and restated bylaws, as they will be in effect immediately prior to the consummation of this offering, will contain provisions that may delay, defer or discourage another party from acquiring control of us. We expect that these provisions, which are summarized below, will discourage coercive takeover practices or inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors, which we believe may result in an improvement of the terms of any such acquisition in favor of our stockholders. However, they also give our board of directors the power to discourage acquisitions that some stockholders may favor. See "Risk Factors—Risks Related to This Offering and Ownership of Our Common Stock— Provisions in

our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock."

Authorized but Unissued Shares

The authorized but unissued shares of our common stock and our preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of the Nasdaq Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Classified Board of Directors

Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes, with the classes as nearly equal in number as possible and each class serving three-year staggered terms. In all other cases and at any other time, directors may only be removed from our board of directors for cause by the affirmative vote of a majority of the shares entitled to vote. See "Management—Composition of our Board of Directors." These provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control of us or our management.

Stockholder Action; Special Meeting of Stockholders

Our amended and restated certificate of incorporation will provide that our stockholders will not be able to take action by written consent for any matter and may only take action at annual or special meetings. As a result, a holder controlling a majority of our capital stock would not be able to amend our amended and restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws, unless previously approved by our board of directors. Our amended and restated certificate of incorporation will further provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer, our president or another officer selected by a majority of our board of directors, thus limiting the ability of a stockholder to call a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

Advance Notice Requirements for Stockholder Proposals and Director Nominations

In addition, our amended and restated bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. In order for any matter to be "properly brought" before a meeting, a stockholder will have to comply with advance notice and duration of ownership requirements and provide us with certain information. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a qualified stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying stockholder actions that are favored by the holders of a majority of our outstanding voting securities until the next stockholder meeting.

Amendment of Certificate of Incorporation or Bylaws

The DGCL provides generally that the affirmative vote of the holders of a majority in voting power of the shares entitled to vote is required to amend a corporation's certificate of incorporation, unless a corporation's certificate of incorporation requires a greater percentage. Upon consummation of this offering, our bylaws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders a majority of the votes which all our stockholders would be eligible to cast in an election of directors.

Section 203 of the DGCL

We are subject to Section 203 of the DGCL, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Limitations on Liability and Indemnification of Officers and Directors

Our amended and restated bylaws provide indemnification for our directors and officers to the fullest extent permitted by the DGCL, along with the right to have expenses incurred in defending proceedings paid in advance of their final disposition. Prior to the consummation of this offering, we intend to enter into indemnification agreements with each of our directors and executive officers that may, in some cases, be broader than the specific indemnification and advancement provisions contained under our amended and restated bylaws and provided under Delaware law. In addition, as permitted by Delaware law, our amended and restated certificate of incorporation includes provisions that eliminate the personal liability of our directors for monetary damages resulting from breaches of certain fiduciary duties as a director. The effect of this provision is to restrict our rights and the rights of our stockholders to recover monetary damages against a director for breach of fiduciary duties as a director.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable.

Dissenters' Rights of Appraisal and Payment

Under the DGCL, with certain exceptions, our stockholders will have appraisal rights in connection with a merger or consolidation of Fractyl Health, Inc. Pursuant to the DGCL, stockholders who properly demand and perfect appraisal rights in connection with such mergers or consolidations will have the right to receive payment of the fair value of their shares as determined by the Delaware Court of Chancery, subject to certain limitations.

Stockholders' Derivative Actions

Under the DGCL, any of our stockholders may bring an action in our name to procure a judgment in our favor, also known as a derivative action, in certain circumstances. Among other things, either the stockholder bringing any such action must be a holder of our shares at the time of the transaction to which the action relates or such stockholder's stock must have thereafter devolved by operation of law, and such stockholder must continuously hold shares through the resolution of such action.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is .

Trading Symbol and Market

We have applied to list our common stock on the Nasdaq Global Market under the symbol "GUTS."

SHARES ELIGIBLE FOR FUTURE SALE

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock. Although we have applied to have our common stock listed on the Nasdaq Global Market, we cannot assure you that there will be an active public market for our common stock.

Upon the closing of this offering, we will have outstanding an aggregate of shares of common stock (shares if the underwriters exercise their option to purchase additional shares from us in full). Of these shares, all shares of common stock sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

Lock-Up Agreements

We, our officers and directors and holders of substantially all of our common stock and securities convertible into or exchangeable for our common stock have agreed that, without the prior written consent of BofA Securities, Inc., Morgan Stanley & Co. LLC and Evercore Group L.L.C., as representatives of the underwriters, we and they will not, subject to certain exceptions, during the period ending 180 days after the date of this prospectus:

- directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, any shares of our common stock, or any securities convertible into or exchangeable for shares of our common stock; or

- enter into any swap or any other agreement or transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock,

whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise. These agreements are subject to certain exceptions, as described in the section of this prospectus entitled "Underwriting."

The representatives of the underwriters have advised us that they have no present intent or arrangement to release any shares subject to a lock-up, and will consider the release of any lock-up on a case-by-case basis. Upon a request to release any shares subject to a lock-up, the representatives of the underwriters would consider the particular circumstances surrounding the request, including, but not limited to, the length of time before the lock-up expires, the number of shares requested to be released, reasons for the request, the possible impact on the market or our common stock and whether the holder of our shares requesting the release is an officer, director or other affiliate of ours.

Upon the expiration of the applicable lock-up periods, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above.

Rule 144

Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days

before a sale, who has beneficially owned shares of our common stock for at least 180 days would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding; and
- the average weekly trading volume in our common stock on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the SEC and Nasdaq concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-Affiliate Resales of Restricted Securities

Under Rule 144, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the 90 days preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of our employees, directors, officers, consultants or advisors who purchases shares from us in connection with a compensatory stock or option plan or other written agreement before the effective date of the registration statement of which this prospectus forms a part is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. Our affiliates can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The SEC has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Registration Rights

Pursuant to our IRA, beginning six months after the completion of this offering, the holders of up to shares of our common stock, or certain transferees, will be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. See the section titled "Description of Capital Stock—Registration Rights" for a description of these registration rights. If the offer and sale of these shares of our common stock are registered, the shares will be freely tradable without restriction under the Securities Act, subject to the Rule 144 limitations applicable to affiliates, and a large number of shares may be sold into the public market.

Registration Statements on Form S-8

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options, warrants and common stock issuable, under our equity incentive plans. We expect to file the registration statement covering shares offered pursuant to these stock plans shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market subject to compliance with the resale provisions of Rule 144.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences for Non-U.S. Holders (as defined below) of the purchase, ownership, and disposition of our common stock issued pursuant to this offering. This discussion does not purport to be a complete analysis of all potential tax effects relating thereto. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local, or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder of our common stock. We have not requested and will not seek any ruling from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership, and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income and the alternative minimum tax. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules under the U.S. federal income tax laws, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle, or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions, regulated investment companies, or real estate investment trusts;
- brokers or dealers in securities or currencies;
- traders in securities or other persons that elect to use a mark-to-market method of accounting for their holdings in our stock;
- controlled foreign corporations (as defined in Section 957 of the Code), passive foreign investment companies (as defined in Section 1297 of the Code), and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes and other pass-through entities (and investors in such entities);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- pension plans or tax-exempt retirement plans;
- persons that own, or are deemed to own, more than five percent of our capital stock;

- "qualified foreign pension funds" as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds; and

- persons subject to special tax accounting rules as a result of any item of gross income with respect to the common stock being taken into account in an applicable financial statement (as defined in Section 451(b) of the Code).

If an entity or arrangement treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership, and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL, OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "United States person" nor an entity treated as a partnership for U.S. federal income tax purposes. A United States person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;

- a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;

- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

- a trust that (1) is subject to the primary supervision of a U.S. court and which has one or more "United States persons" (as defined in Section 7701(a)(30) of the Code) that have the authority to control all substantial decisions of the trust, or (2) has a valid election in effect to be treated as a United States person under the applicable Treasury Regulations.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "—Sale or other taxable disposition."

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the

dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder timely furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may be able to obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder generally will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must timely furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular rates applicable to United States persons. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate provided for by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

Subject to the discussion below on information reporting, backup withholding and foreign accounts, a Non-U.S. Holder will generally not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);

- the Non-U.S. Holder is a nonresident alien individual present in the United States for a period or periods aggregating 183 days or more during the taxable year of the disposition and certain other requirements are met; or

- our common stock constitutes a U.S. real property interest, or a USRPI, by reason of our status as a U.S. real property holding corporation, or a USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the rates applicable to United States persons. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate provided for by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A Non-U.S. Holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate provided for by an applicable income tax treaty) on gain realized upon the sale or other taxable disposition of our common stock, which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other

business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock, if any, will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by timely furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any distributions on our common stock paid to the Non-U.S. Holder, regardless of whether such distributions constitute dividends or whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA), on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock. The U.S. Department of the Treasury has issued proposed Treasury Regulations providing that the withholding provisions under FATCA do not apply with respect to the gross proceeds from a sale or other disposition of our common stock. In its preamble to such proposed regulations, the U.S. Department of the Treasury stated that taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

UNDERWRITING

BofA Securities, Inc., Morgan Stanley & Co. LLC and Evercore Group L.L.C. are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
BofA Securities, Inc.	
Morgan Stanley & Co. LLC	
Evercore Group L.L.C.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $ million and are payable by us. We have also agreed to reimburse the underwriters for their expenses relating to clearance of this offering with the Financial Industry Regulatory Authority in an amount up to $.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 180 days after the date of this prospectus without first obtaining the written consent of the representatives. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock;
- exercise any right with respect to the registration of any of the common stock, or file, cause to be filed or cause to be confidentially submitted any registration statement in connection therewith; or
- enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the common stock, whether any such swap or transaction is to be settled by delivery of shares of common stock or other securities, in cash or otherwise.

The exceptions to the restrictions in the immediately preceding paragraph permit our executive officers and directors, subject to certain restrictions, to transfer the common stock:

- as a bona fide gift or gifts;
- to any immediate family member or any trust;
- as a distribution to any limited partners, members, stockholders or other equity holders;
- to affiliates or to any investment fund or other entity controlled or managed by the person subject to the lock-up;
- by will or intestate succession; or
- pursuant to a court order, a qualified domestic order or in connection with a divorce settlement.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Nasdaq Global Market Listing

We have applied to list our common stock on the Nasdaq Global Market under the symbol "GUTS."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us,
- our financial information,
- the history of, and the prospects for, our company and the industry in which we compete,
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues,
- the present state of our development, and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a

decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

European Economic Area and the United Kingdom

In relation to each Member State of the European Economic Area and the United Kingdom (each a "Relevant State"), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation), except that offers of Shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

a. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;

b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of coordinator for any such offer; or

c. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of Shares shall require the Issuer or any Manager to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the underwriters that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any Shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

References to the Prospectus Regulation includes, in relation to the UK, the Prospectus Regulation as it forms part of UK domestic law by virtue of the European Union (Withdrawal) Act 2018.

The above selling restriction is in addition to any other selling restrictions set out below.

In connection with the offering, the underwriters are not acting for anyone other than the issuer and will not be responsible to anyone other than the issuer for providing the protections afforded to their clients nor for providing advice in relation to the offering.

Notice to Prospective Investors in the United Kingdom

In relation to the United Kingdom, or the UK, no Shares have been offered or will be offered pursuant to the offering to the public in the UK prior to the publication of a prospectus in relation to the Shares which has been approved by the Financial Conduct Authority in the UK in accordance with the UK Prospectus Regulation and the FSMA, except that offers of Shares may be made to the public in the UK at any time under the following exemptions under the UK Prospectus Regulation and the FSMA:

a. to any legal entity which is a qualified investor as defined under the UK Prospectus Regulation;

b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the UK Prospectus Regulation), subject to obtaining the prior consent of coordinator for any such offer; or

c. at any time in other circumstances falling within section 86 of the FSMA,

provided that no such offer of Shares shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or Article 3 of the UK Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

Each person in the UK who initially acquires any Shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the Managers that it is a qualified investor within the meaning of the UK Prospectus Regulation.

In the case of any Shares being offered to a financial intermediary as that term is used in Article 5(1) of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the Shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in the UK to qualified investors, in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The Company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any Shares in the UK means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares, the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018, and the expression "FSMA" means the Financial Services and Markets Act 2000.

In connection with the offering, the underwriters are not acting for anyone other than the issuer and will not be responsible to anyone other than the issuer for providing the protections afforded to their clients nor for providing advice in relation to the offering.

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the "Financial Promotion Order"), (ii) are persons falling within Article 49(2)(a) to (d) ("high net worth companies, unincorporated associations etc.") of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, as amended ("FSMA")) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as "relevant persons"). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or the DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or the Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons, or the Exempt Investors, who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, the shares were not offered or sold or caused to be made the subject of an invitation for subscription or purchase and will not be offered or sold or caused to be made the subject of an invitation for subscription or purchase, and this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares, has not been circulated or distributed, nor will it be circulated or distributed, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time, or the SFA) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a. a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

b. a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

a. to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

b. where no consideration is or will be given for the transfer;

c. where the transfer is by operation of law; or

d. as specified in Section 276(7) of the SFA.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of

the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* NI 33-105, the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Latham & Watkins LLP. Goodwin Procter LLP has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERT

The consolidated financial statements of Fractyl Health, Inc. at December 31, 2021 and 2020, and for each of the two years in the period ended December 31, 2021, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed with the registration statement. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits filed with the registration statement. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. The SEC also maintains an internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that website is *www.sec.gov*.

Upon the closing of this offering, we will be required to file periodic reports, proxy statements, and other information with the SEC pursuant to the Exchange Act. These reports, proxy statements, and other information will be available on the website of the SEC referred to above.

We also maintain a website at *www.fractyl.com*, through which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on or accessed through our website is not a part of this prospectus and the inclusion of our website address in this prospectus is an inactive textual reference only.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Fractyl Health, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Fractyl Health, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Boston, Massachusetts
April 4, 2022

Fractyl Health, Inc.
Consolidated Balance Sheets
(in thousands, except for share and per share information)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 95,473	$ 29,107
Prepaid expenses and other current assets	915	1,775
Total current assets	96,388	30,882
Property and equipment, net	723	1,356
Right-of-use lease assets	622	—
Other long-term assets	4,815	2,522
Total assets	$ 102,548	$ 34,760
Liabilities, Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable	$ 970	$ 304
Accrued expenses and other current liabilities	6,010	2,913
Deferred rent, current	—	530
Lease liabilities, current	950	—
Note payable, current	15,724	7,174
Total current liabilities	23,654	10,921
Deferred rent, long-term	—	750
Lease liabilities, long-term	334	—
Note payable, long-term	—	8,119
Convertible preferred stock warrant liability	544	188
Other long-term liabilities	11	19
Total liabilities	24,543	19,997
Commitments and contingencies		
Convertible preferred stock (Series A, B, C-1, C-2, D, E and F), $0.00001 par value; 78,112,639 and 70,832,388 shares authorized at December 31, 2021 and 2020, respectively; 77,994,156 and 66,067,108 shares issued and outstanding at December 31, 2021 and 2020, respectively; aggregate liquidation preference of $344,734 and $230,258 at December 31, 2021 and 2020, respectively	287,330	187,484
Stockholders' deficit:		
Common stock, $0.00001 par value; 107,000,000 and 96,000,000 shares authorized at December 31, 2021 and 2020, respectively; 4,049,782 and 3,978,326 shares issued and outstanding at December 31, 2021 and 2020, respectively	—	—
Additional paid-in capital	13,747	11,616
Accumulated deficit	(223,072)	(184,337)
Total stockholders' deficit	(209,325)	(172,721)
Total liabilities, convertible preferred stock and stockholders' deficit	$ 102,548	$ 34,760

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except for share and per share information)

	Year Ended December 31,	
	2021	2020
Operating expenses:		
Research and development	$ 26,435	$ 22,433
General and administrative	10,493	6,528
Total operating expenses	36,928	28,961
Loss from operations	(36,928)	(28,961)
Other expenses, net:		
Interest expense, net	(1,442)	(1,503)
Change in fair value of convertible preferred stock warrant liability	(356)	(15)
Other expenses, net	(9)	(1)
Total other expenses, net	(1,807)	(1,519)
Net loss and comprehensive loss	(38,735)	(30,480)
Accretion of dividends on convertible preferred stock	(14,486)	(10,422)
Net loss attributable to common stockholders	$ (53,221)	$ (40,902)
Net loss per share attributable to common stockholders, basic and diluted	$ (13.34)	$ (10.34)
Weighted-average number of common shares outstanding, basic and diluted	3,990,680	3,955,147

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except for share and per share information)

	Series A, B, C-1, C-2, D, E and F Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balance at December 31, 2019	53,228,535	$ 133,111	3,912,496	$ —	$ 9,861	$ (153,857)	$ (143,996)
Issuance of Series E convertible preferred stock, net of issuance costs of $695	12,838,573	54,373	—	—	—	—	—
Exercise of common stock options	—	—	65,830	—	24	—	24
Stock-based compensation expense	—	—	—	—	1,626	—	1,626
Issuance of common stock warrants	—	—	—	—	105	—	105
Net loss	—	—	—	—	—	(30,480)	(30,480)
Balance at December 31, 2020	66,067,108	187,484	3,978,326	—	11,616	(184,337)	(172,721)
Issuance of Series F convertible preferred stock, net of issuance costs of $154	11,927,048	99,846	—	—	—	—	—
Exercise of common stock options	—	—	71,456	—	40	—	40
Stock-based compensation expense	—	—	—	—	2,091	—	2,091
Net loss	—	—	—	—	—	(38,735)	(38,735)
Balance at December 31, 2021	77,994,156	$ 287,330	4,049,782	$ —	$ 13,747	$ (223,072)	$ (209,325)

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Consolidated Statements of Cash Flows
(in thousands, except for share and per share information)

	Year Ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	$(38,735)	$(30,480)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	676	770
Loss on disposal of fixed assets	8	—
Stock-based compensation expense	2,091	1,626
Non-cash interest expense	431	502
Change in fair value of convertible preferred stock warrant liability	356	15
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	860	(789)
Accounts payable	666	(304)
Accrued expenses and other current liabilities	3,097	614
Deferred rent	—	(499)
Lease assets and lease liabilities, net	(618)	—
Other long-term assets and liabilities	(2,294)	(2,528)
Net cash used in operating activities	(33,462)	(31,073)
Cash flows from investing activities:		
Purchases of property and equipment	(51)	(2)
Net cash used in investing activities	(51)	(2)
Cash flows from financing activities:		
Proceeds from issuance of convertible preferred stock, net of issuance costs	99,846	54,373
Proceeds from exercise of stock options	40	24
Principal payments on capital lease obligations	(7)	(7)
Net cash provided by financing activities	99,879	54,390
Net increase in cash, cash equivalents and restricted cash	66,366	23,315
Cash, cash equivalents and restricted cash at beginning of period	29,107	5,792
Cash, cash equivalents and restricted cash at end of period	$ 95,473	$ 29,107
Supplemental disclosure of cash flow information:		
Interest paid	$ 1,028	$ 1,039
Non-cash investing and financing activities:		
Issuance of common stock warrants in connection with long-term debt	$ —	$ 105

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Notes to Consolidated Financial Statements
(in thousands, except share and per share information)

1. Nature of the Business and Basis of Presentation

Fractyl Health, Inc. (the "Company") was incorporated on August 30, 2010 under the name MedCatalyst, Inc. The Company subsequently changed its name to Fractyl Laboratories Inc. on January 10, 2012 and subsequently to Fractyl Health, Inc. on June 9, 2021. The Company is an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes ("T2D"). The Company's goal is to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. The Revita DMR System ("Revita"), the Company's lead product candidate, is designed to remodel the duodenal lining via hydrothermal ablation in order to edit abnormal intestinal nutrient sensing and signaling mechanisms that it believes are a root cause of metabolic diseases. Led by the Company's ongoing Revitalize-1 pivotal study, the Company has initiated a broad clinical program, Revitalize T2D, designed to evaluate Revita in multiple concurrent clinical studies across a range of patient populations from prediabetes to T2D patients on long-acting insulin. In addition, the Company is developing Rejuva, a novel pancreatic gene therapy platform, to enable long-term remission of T2D by potentially restoring insulin production in patients with advanced disease. The Company believes its product candidates have the capacity to revolutionize the treatment of T2D, align the interest of key stakeholders in the disease, and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

The accompanying consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs"), promulgated by the Financial Accounting Standards Board ("FASB").

Liquidity

Under ASC 205-40, *Going Concern*, management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved by the Company's Board of Directors ("Board") before the date that the financial statements are issued.

The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. The Company is subject to a number of risks similar to other early-stage life science companies, including, but not limited to, successful discovery and development of its product candidates, raising additional capital with favorable terms, development by its competitors of new technological innovations, protection of proprietary technology and market acceptance of the Company's products. The successful discovery and development of product candidates requires substantial working capital which may not be available to the Company on favorable terms or not at all. The costs of the Revitalize-2 pivotal study, Revitalize-3 pilot study and the continued preclinical development of the Rejuva gene therapy platform are planned to be financed with the proceeds from the Company's anticipated future financing.

To date, the Company has no revenue from product sales and management expects continuing operating losses in the future. The Company has financed its operations to date primarily through sales of its convertible preferred stock and debt financing. As of December 31, 2021, the Company had cash and cash equivalents totaling $95,473, net working capital of $72,734 and an accumulated deficit of $223,072. The Company believes that its cash and cash equivalents at December 31, 2021 will be sufficient to fund the Company's current operating plan for at least twelve months from the issuance date of the consolidated financial statements.

Impact of COVID-19 Pandemic

In December 2019, SARS-CoV-2, a novel strain of coronavirus that causes COVID-19, was first identified globally. On March 11, 2020, the World Health Organization declared COVID-19 a global pandemic. Since then, COVID-19 has caused significant disruptions and adverse economic impacts across multiple countries, including the United States. To date, the Company has maintained uninterrupted business operations. The Company has implemented adjustments to its operations designed to keep employees safe and comply with federal, state and local guidelines, including those regarding social distancing, and has transitioned administrative functions to predominantly remote work.

Beginning in March 2020 and continuing through the end of 2021, the ongoing COVID-19 pandemic has reduced patient access to clinical laboratories, causing a decrease in enrollment and a temporary suspension of certain trials. The extent to which COVID-19 may further impact the Company's business, results of operations, financial condition and cash flows will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

2. Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates relied upon in preparing these consolidated financial statements include, but are not limited to, the fair value of common stock, the fair value of preferred and common stock warrants, the fair value of stock-based awards, the incremental borrowing rate for lease accounting and the accrual of research and development expenses. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ materially from those estimates. The Company has also considered the potential impact of the COVID-19 pandemic on its estimates and assumptions. The extent to which the COVID-19 pandemic may impact the Company's estimates in future periods is uncertain and subject to change.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated.

Cash and Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at the date of purchase to be cash equivalents. Cash equivalents, which consist of money market funds, are stated at fair value.

Restricted Cash

The Company opened a cash collateral account with a bank in June 2018 in conjunction with the maintenance of two letters of credit required under its facility leases. Both letters of credit were issued for an

original effective period of 12 months with automatic annual renewal until the expiration dates, respectively. In August 2020, the bank lifted the cash collateral requirement associated with the letters of credit and released the cash maintained in the cash collateral account to the Company's operating account.

Concentration of Credit Risk

The Company's financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. Substantially all of the Company's cash deposits are maintained at one large, creditworthy financial institution. The Company's deposits at times may significantly exceed federally insured limits. The Company has not experienced any losses related to its cash and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision-maker, the Company's chief executive officer, views the Company's operations and manages its business as a single operating segment. All of the Company's long-lived assets are held in the United States.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation and amortization expense is recognized using the straight-line method over the following estimated useful lives:

Asset Category	Estimated Useful Life
Computer and office equipment	3 to 5 years
Laboratory and manufacturing equipment	3 years
Website development costs	3 years
Leasehold improvements	Shorter of remaining lease term or the estimated useful life of 5 to 8 years

Costs of major additions and betterments are capitalized and amortized on a straight-line basis over the shorter of the remaining lease term or the estimated useful life of the asset. Upon retirement or sale, the cost of assets disposed of and the related accumulated amortization are removed from the accounts and any resulting gain or loss is included in the determination of net income or loss. Repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist primarily of property and equipment and right-of-use operating lease assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

Deferred Public Offering Costs

Deferred public offering costs, which primarily consist of direct, incremental legal and accounting fees relating to the planned Initial Public Offering ("IPO"), are capitalized within other long-term assets. The deferred public offering costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. The Company had incurred $2,195 in IPO costs as of December 31, 2021. No IPO related costs were incurred as of December 31, 2020.

Other Long-term Assets

At December 31, 2021, other long-term assets consisted of vendor deposits of $2,562, deferred public offering costs of $2,195 and long-term prepaid expenses of $58. At December 31, 2020, other long-term assets represented entirely vendor deposits.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents and convertible preferred stock warrant liability are carried at fair value, determined according to the fair value hierarchy above (See Note 3). The carrying values of the Company's accounts payable and accrued expenses approximate their fair value due to the short-term nature of these liabilities. The carrying value of the Company's outstanding notes payable approximates fair value (a Level 2 fair value measurement), reflecting interest rates currently available to the Company (See Note 6).

Leases

The Company adopted ASC 842, *Leases*, with an initial application date of January 1, 2021, using the modified retrospective method. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, *Leases* ("ASC 840").

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company's finance lease is immaterial.

At the lease commencement date, the Company recognizes a right-of-use asset and a lease liability for all leases, except short-term leases with an original term of 12 months or less. The Company typically only includes

an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is a reasonable certainty that the Company will renew. The operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of fixed lease payments over the expected lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in the lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. The Company recognizes operating lease expense on a straight-line basis over the lease term.

Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

See Note 7—"Leases" and Note 9—"Commitments and Contingencies" for additional information about the Company's leases**.**

Debt Issuance Costs

Debt issuance costs are recorded as a direct reduction to the carrying amount of the related debt liability rather than an asset in accordance with the simplified presentation of debt issuance costs provided by ASU No. 2015-03, *Interest – Imputation of Interest*. Debt issuance costs are amortized as additional interest expense using the effective interest rate method over the term of the debt.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include salaries, stock-based compensation and employee-related benefits, product development, clinical trial and related clinical manufacturing costs, allocation of facility-related expenses, overhead expenses and other outside expenses. Nonrefundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with companies and individuals globally. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or projects, including the phase or completion of events, invoices received and contracted costs. Judgments and estimates are made in determining the accrued balance at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

Convertible Preferred Stock Warrant Liability

The Company classifies a warrant to purchase shares of its Series B convertible preferred stock as a liability on its consolidated balance sheets as the warrant is a free-standing financial instrument that may require the Company to transfer assets upon exercise. The warrant was initially recorded at fair value on the grant date, and it is subsequently remeasured to fair value at each balance sheet date. Changes in fair value of the warrant are recognized as a component of other expenses, net in the consolidated statements of operations and comprehensive loss. The Company will continue to adjust the liability until the earlier of exercise or expiration of the warrant.

The Company uses the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the convertible preferred stock warrant. The Company has assessed these assumptions and estimates at each financial reporting period as additional information impacting the assumptions is obtained. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying Series B convertible preferred stock, the remaining contractual term of the warrant, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying convertible preferred stock. The Company determines the fair value per share of the underlying convertible preferred stock by taking into consideration the most recent sales of its convertible preferred stock, results obtained from third-party valuations and additional factors that are deemed relevant. The Company historically has been a private company and lacks company-specific historical and implied volatility information of its stock. Therefore, it estimates its expected stock volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrant. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrant. Expected dividend yield is determined considering that the underlying Series B convertible preferred stock is entitled to dividends of 6.0% per year, whether or not declared.

Stock-Based Compensation

The Company measures all stock options and other stock-based awards based on their fair value on the date of the grant. Those awards typically have a graded vesting schedule and compensation expense for awards with only service conditions are recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. Compensation costs recognized for performance-based awards reflect the number of awards that are expected to vest during the requisite service period, and are adjusted to reflect those awards that ultimately vest upon final determination of the performance conditions achieved. Historical performance patterns, to the extent that they are indicative to the performance conditions to be achieved, are used in developing estimates for the probability of attaining these performance conditions.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient’s payroll costs are classified or in which the award recipient’s service payments are classified.

The Company uses the Black-Scholes option pricing model, which incorporates assumptions and estimates, to measure the fair value of its option awards on the date of grant of each stock option award. The Company determines the fair value per share of the underlying common stock by taking into consideration the results obtained from third-party valuations and additional factors that are deemed relevant. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, the Company estimates its expected stock volatility based on an analysis of reported data for a publicly traded peer group of companies that granted options with substantially similar terms and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term assumption for employee grants is determined by using the “simplified” method for awards that qualify as “plain-vanilla” options. The risk-free interest rate is based on the rate of the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future. Forfeitures are accounted for as they occur.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and the tax basis of existing assets and liabilities and for loss and credit carryforwards using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Comprehensive Loss

Comprehensive loss is comprised of two components: net loss and other comprehensive loss, which includes other changes in stockholders' deficit that result from transactions and economic events other than those with stockholders. The Company had no items qualifying as other comprehensive loss; accordingly, comprehensive loss equaled total net loss for each of the years ended December 31, 2021 and 2020.

Net Loss Per Share

Net loss per share attributable to common stockholders is calculated using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company's common shares and participating securities. The Company's Series A, Series B, Series C-1, Series C-2, Series D, Series E, and Series F convertible preferred stock contain participating rights in any dividend paid by the Company and are therefore participating securities. Net loss attributable to common stockholders and participating securities is allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. However, the participating securities do not include a contractual obligation to share in the losses of the Company and were not included in the calculation of net loss per share in the periods that had a net loss.

Basic net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the if-converted method and treasury stock method, as applicable. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. Diluted net loss per share is equivalent to basic net loss per share for the years presented herein because common stock equivalent shares from the Series A, Series B, Series C-1, Series C-2, Series D, Series E, and Series F convertible preferred stock, stock option awards and outstanding warrants to purchase common stock and convertible preferred stock (see Note 17) were anti-dilutive.

Emerging Growth Company Status

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. The Company may take advantage of these exemptions until the Company is no longer an "emerging growth company." Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards and as a result of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of an offering or such earlier time that it is no longer an "emerging growth company".

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASC 842, *Leases* ("ASC 842"). Under this new guidance, lessees are required to recognize a right-of-use asset and a lease liability for virtually all of their leases (other than leases that meet the definition of a short-term lease), however, the expense recognition model is similar to the previous guidance. The liability is measured at the present value of the fixed lease payments over the lease term and the right-of-use ("ROU") asset is measured at the lease liability amount, subject to certain adjustments, such as for initial direct costs.

The Company adopted this new accounting standard on January 1, 2021 using the modified retrospective approach. As part of the adoption, the Company elected the package of practical expedients permitted under the transition guidance, which among other things, permits the carry forward of historical lease classifications. In addition, the Company elected the practical expedient not to apply the recognition requirements of the lease standard to short-term leases (a lease that at commencement date has a lease term of 12 months or less and does not contain a purchase option that is reasonably certain to exercise) and the practical expedient that permits lessees to make an accounting policy election (by class of underlying asset) to account for each separate lease component of a contract and its non-lease components as a single lease component. Upon adoption of ASC 842, the Company recognized $1,010 of operating lease ROU assets and $2,290 of operating lease liabilities. The difference between the additional operating lease ROU assets and operating lease liabilities, is primarily due to the change in classification of lease incentives from liabilities to a reduction in operating lease ROU assets. The adoption of the standard did not have a material impact on the Company's operating results or cash flows. The following table summarizes the effect on the Company's Consolidated Balance Sheet upon its adoption of ASC 842 on January 1, 2021:

Financial Statement Line Item	As reported January 1, 2021	Adoption Adjustment	As adjusted January 1, 2021
Right-of-use lease assets	$ —	$ 1,010	$ 1,010
Deferred rent, current	530	(530)	—
Lease liabilities, current	—	1,008	1,008
Deferred rent, long-term	750	(750)	—
Lease liabilities, long-term	$ —	$ 1,282	$ 1,282

See Note 7—"Leases" and Note 9—"Commitments and Contingencies" for additional information about the Company's leases.

Recently Issued Accounting Pronouncements—Not Adopted as of December 31, 2021

In December 2019, the FASB issued ASU 2019-12, *Income Taxes—Simplifying the Accounting for Income Taxes*. The ASU simplifies the accounting for income taxes by removing certain exceptions to the general principles

as well as clarifying and amending existing guidance to improve consistent application. The amendments under ASU 2019-12 are effective for fiscal years beginning after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022, with early adoption permitted. Depending on the amendment, adoption may be applied on the retrospective, modified retrospective or prospective basis. The Company is currently assessing the potential impact of adopting ASU 2019-12 on its financial statements and related disclosures.

In August 2020, the FASB issued ASU 2020-06, ASC Subtopic 470-20 Debt-Debt with Conversion and Other Options and ASC subtopic 815-40 Hedging-Contracts in Entity's Own Equity. The ASU reduced the number of accounting models for convertible debt instruments and convertible preferred stock. Convertible instruments that continue to be subject to separation models are (1) those with embedded conversion features that are not clearly and closely related to the host contract, that meet the definition of a derivative, and that do not qualify for a scope exception from derivative accounting; and, (2) convertible debt instruments issued with substantial premiums for which the premiums are recorded as paid-in capital. The amendments in this update are effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is currently assessing the potential impact of adopting ASU 2020-06 on its financial statements and related disclosures.

In October 2020, the FASB issued ASU No. 2020-10, *Codification Improvements* ("ASU 2020-10"). The ASU contains improvements to the Codification by ensuring that all guidance that requires or provides an option for an entity to provide information in the notes to financial statements is codified in the disclosure section of the Codification. The ASU also improves various topics in the Codification so that entities can apply guidance more consistently on codifications that are varied in nature where the original guidance may have been unclear. The amendments in ASU 2020-10 are effective for the Company for fiscal years beginning after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022. Early adoption is permitted. The Company is currently assessing the potential impact of adopting ASU 2020-10 on its financial statements and related disclosures.

3. Fair Value Measurements

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of fair value hierarchy utilized to determine such fair values:

	Fair Value measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents—money market funds	$ 2	$ —	$ —	$ 2
	$ 2	$ —		$ 2
Liabilities:				
Convertible preferred stock warrant liability	$ —	$ —	$ 544	$544
	$ —	$ —	$ 544	$544

	Fair Value measurements as of December 31, 2020			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents—money market funds	$10,902	$ —	$ —	$10,902
	$10,902	$ —	$ —	$10,902
Liabilities:				
Convertible preferred stock warrant liability	$ —	$ —	$ 188	$ 188
	$ —	$ —	$ 188	$ 188

During the years ended December 31, 2021 and 2020, there were no transfers between Level 1, Level 2 and Level 3.

Due to the lack of market quotes relating to the Company's convertible preferred stock warrants, the fair value of the convertible preferred stock warrants was determined as of December 31, 2021 and 2020 using the Black-Scholes model, which is based on Level 3 inputs (See Note 8). The following table provides a rollforward of the fair value of the Company's warrant liability:

	Fair Value
Balance as of December 31, 2020	$188
Increase in fair value	356
Balance as of December 31, 2021	$544

4. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2021	2020
Computer and office equipment	$ 927	$ 1,048
Laboratory and manufacturing equipment	812	867
Website development costs	40	36
Leasehold improvements	3,473	3,467
	5,252	5,418
Less: accumulated depreciation	(4,529)	(4,062)
	$ 723	$ 1,356

Depreciation expense for the years ended December 31, 2021 and 2020 were $676 and $770, respectively.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31,	
	2021	2020
External research and development services	$1,784	$1,538
Payroll and payroll-related expenses	1,851	982
Professional fees and consulting services	2,272	251
Other current liabilities	103	142
	$6,010	$2,913

6. Notes Payable

2019 Note

In February 2019, the Company entered into a loan and security agreement (the "2019 Note") with a lender that provided for borrowings of up to $15,000 in two term loan advances defined as "Term A Loan" and "Term B Loan", collectively referred to as "Term Loans". Under Term A Loan, the Company may borrow up to $10,000 by June 30, 2019 with an initial draw of $3,000 upon execution of the 2019 Note and optional additional borrowings at a minimum increment of $2,500. Under Term B Loan, the Company may borrow $5,000 upon achieving certain clinical milestones as defined in the 2019 Note, by December 31, 2019. On February 5, 2019, the Company drew down $3,000 under Term A Loan, and on May 31, 2019, the Company drew down an additional $7,000 under Term A Loan. On October 3, 2019, the Company drew down $5,000 under Term B Loan.

The outstanding balances under the Term Loans bear interest at a floating annual rate that equals the greater of 1.5% above the Wall Street Journal prime rate or 6.75%. The Term Loans initially required interest-only repayments through December 31, 2020. After the interest-only period, the Term Loans require 24 equal monthly principal repayments of the outstanding balances plus accrued interest through the maturity date on December 1, 2022. Borrowings under the 2019 Note are secured by substantially all assets of the Company and assets the Company may acquire in the future, other than intellectual property, except for proceeds from intellectual property outstanding.

There are no financial covenants associated with the 2019 Note; however, there are certain operating and negative covenants restricting the Company's activities, including limitations on dispositions, mergers or acquisitions, encumbering or granting a security interest in its intellectual property, incurring indebtedness or liens, paying dividends, making certain investments and engaging in certain other business transactions. The obligations under the 2019 Note are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in the Company's business, operations or financial or other condition.

The 2019 Note provides for certain prepayment premiums should the Company make early payments of any principal balances prior to the maturity date. Upon occurrence of either payment default or covenant default, the lender may take one of the following actions: i) declare that all obligations are immediately due and payable; ii) stop advancing money; iii) demand that the Company deposit cash collateral with the lender.

On the date that the 2019 Note is paid in full or becomes due and payable, the Company will make a payment (the "Final Payment"), in addition to the regular monthly payments of principal plus accrued interest, equal to 6% of the original principal amount of the Term Loans extended by the lender. The Final Payment is being accreted as additional interest expense over the term of the respective Term Loans using the effective interest rate method.

In February 2019, in connection with entering into the 2019 Note, the Company issued to the lender and an affiliated investor warrants to purchase up to an aggregate of 257,380 shares of the Company's common stock with par value of $0.00001 per share, at an exercise price of $1.55 per share (the "2019 Warrants"). Of the 257,380 shares, 171,606 shares were exercisable upon the issuance of the warrants and an additional 85,774 shares became exercisable upon the drawdown of the Term B Loan. The warrants have a contractual term of ten years from issuance. The Company recorded the total fair value of the warrants of $284 as debt discount and additional paid-in capital. The debt discount recorded by the Company also included $24 of fees paid to lenders and $25 of debt issuance costs. The debt discount is being amortized as additional interest expense over the term of the respective Term Loans using the effective interest rate method. The 2019 Warrants were not exercised from its inception through December 31, 2021.

First Amendment to 2019 Note

On December 31, 2020, the Company entered into the First Amendment to the 2019 Note (the "First Amendment") whereby the Term Loans were amended to revise the interest-only repayment terms.

The First Amendment extended interest-only payments through January 31, 2021. After the interest-only period, the First Amendment requires 23 equal monthly principal repayments of the outstanding balance plus accrued interest starting from February 1, 2021 through the maturity date of December 1, 2022. Upon achieving certain milestones as specified in the First Amendment, the interest-only payment may be extended through July 31, 2021 with the principal to be repaid equally over 17 consecutive calendar months starting August 1, 2021 and may be further extended through December 31, 2021 with principal to be repaid equally over 12 consecutive calendar months starting January 1, 2022.

In connection with entering into the First Amendment, the Company issued to the lender and an affiliated investor, warrants to purchase up to an aggregate of 89,452 shares of the Company's common stock, par value $0.00001 per share, at an exercise price of $1.81 per share (the "2020 Warrants"). The 2020 Warrants expire ten years from the date of issuance on December 30, 2030.

The Company accounted for the First Amendment as a debt modification in accordance with ASC 470-50, *Modifications and Extinguishments*. As such, unamortized fees will continue to be deferred and amortized, any new creditor fees were capitalized and amortized as part of the effective yield and new fees paid to third parties were expensed.

The Company recorded the total fair value of the 2020 Warrants of $105 as debt discount and additional paid-in capital. The debt discount recorded by the Company also included $8 of debt issuance costs. The debt discount was being amortized as additional interest expense over the term of the respective Term Loans using the effective interest rate method. The 2020 Warrants were not exercised through December 31, 2021.

The fair value of the 2020 Warrants was determined using the Black-Scholes option-pricing model with the following assumptions:

Risk-free interest rate	0.9%
Weighted average expected term (in years)	10.0
Weighted average expected volatility	57%
Weighted average expected dividend yield	0%
Fair value of common stock per share	$1.81

Second Amendment to 2019 Note

On February 26, 2021, the Company entered into the Second Amendment to the 2019 Note (the "Second Amendment") to further revise the interest-only repayment terms amended by the First Amendment.

The Second Amendment extended interest-only payments through July 31, 2021, upon the achievement of a certain milestone event, as defined in the Second Amendment. After the interest-only period, the Second Amendment requires 17 equal monthly principal repayments of the outstanding balance plus accrued interest through the maturity date of December 1, 2022. Upon achieving additional milestone events as specified in the Second Amendment, the interest-only payment may be extended to December 31, 2021, with principal to be repaid equally over 12 consecutive calendar months through the maturity date of December 1, 2022.

The Company accounted for the Second Amendment as a debt modification in accordance with ASC 470-50, *Modifications and Extinguishments*. As such, unamortized fees will continue to be deferred and amortized. New creditor fees related to the Second Amendment were immaterial.

In June 2021, upon achievement of certain milestones in the Second Amendment, the interest-only payment was extended through January 1, 2022. All principal under the Term Loans will be repaid over 12 consecutive calendar months in the year ending December 31, 2022.

For the years ended December 31, 2021 and 2020, the Company recognized total interest expense of $1,457 and $1,531 respectively, related to the 2019 Note, which included additional interest expense of $431 and $502, respectively, associated with the accretion of the Final Payment and the amortization of the debt discount. The effective annual interest rate of the 2019 Note was 9.72% and 9.96% for the year ended December 31, 2021 and 2020, respectively.

On January 3, 2022, the Company fully paid off the 2019 Note by making a lump-sum payment to the lender of the Term Loans for a total amount of $16,130, which consisted of the outstanding principal balance of the Term Loans of $15,000, the Final Payment of $900, the prepayment premium of $137 and accrued interest of $93.

7. Leases

In November 2015, the Company entered into a lease agreement for office and laboratory space in Lexington, Massachusetts with the lease term covering a seven-year period from May 1, 2016 through April 30, 2023 (the “Lexington Lease”). The Lexington facility includes 30,000 square feet of office and laboratory space and has been occupied by the Company since August 2016. The Lexington Lease includes a provision for a $3,000 tenant improvement allowance, which was funded by the landlord in 2016. The Lexington Lease does not contain any material residual value guarantees or material restrictive covenants.

The Company recognized right-of-use assets and lease liabilities for such leases in connection with its adoption of ASC 842 as of January 1, 2021 (see Note 2 – “Recently Adopted Accounting Pronouncements” for more information). The Company reports operating lease right-of-use assets in right-of-use lease assets and the current and non-current portions of its operating lease liabilities in lease liabilities, current and lease liabilities, long-term, respectively, on its Consolidated Balance Sheet. The discount rate used to calculate lease liabilities was the Company’s estimated incremental borrowing rate of 6.75%.

As of December 31, 2021, the Company’s Lexington Lease has a remaining term of 16 months. The term of the Company’s lease of office and laboratory space for its headquarters in Lexington, Massachusetts includes options for a five-year and three-year extension period that the Company is not reasonably certain to exercise. The Company is not involved in the construction or design of the additional underlying asset, aside from constructing leasehold improvements. The following table is a summary of the components of lease costs included in research and development and general and administrative expenses for the year ended December 31, 2021:

	2021
Operating lease cost	$510
Variable lease costs	234
Total lease cost	$744

Supplemental cash flow information related to leases for the year ended December 31, 2021 is as follows:

	2021
Operating cash flows paid for operating leases	$1,043

See Note 9 “Commitments and Contingencies” for additional information about the Company’s leases.

8. Convertible Preferred Stock Warrant Liability

In January 2014, the Company issued a fully vested warrant to purchase 118,483 shares of the Company’s Series B convertible preferred stock in connection with the 2014 Note. The warrant was immediately exercisable at an exercise price of $1.266 per share and has a contractual term of ten years from issuance. The fair value of the warrant at issuance was $48 and was recorded as a convertible preferred stock warrant liability. This amount was recorded as a debt discount and was being amortized to interest expense over the term of the note. The warrant was not exercised from its inception through December 31, 2021.

The Company re-measures the fair value of the liability for this convertible preferred stock warrant at each reporting date, with any adjustments being recorded as a component of other expenses in the Company’s consolidated statements of operations and comprehensive loss. The Company recorded related expense of $356 and $15 for the years ended December 31, 2021 and 2020, respectively.

The estimated fair value of the outstanding warrant was $544 and $188 as of December 31, 2021 and 2020, respectively. The fair value was determined using the Black-Scholes option-pricing model with the following assumptions:

	Years Ended December 31,	
	2021	2020
Risk-free interest rate	0.7%	0.2%
Expected term (in years)	2.1	3.1
Expected volatility	66%	64%
Expected Dividend yield	6%	6%
Fair value of Series B convertible preferred stock per share	$6.55	$3.06

9. Commitments and Contingencies

Operating Lease Commitments

The following table summarizes the maturity of lease liabilities under operating leases as of December 31, 2021:

Year Ending December 31,	
2022	$ 983
2023	360
Total future minimum lease payments	1,343
Less: Imputed interest	59
Total lease liabilities	$1,284

Guarantees and Indemnification Obligations

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to these agreements, the Company indemnifies and agrees to reimburse the indemnified party for losses and costs incurred by the indemnified party in connection with any patent, copyright, trade secret or other intellectual property

or personal right infringement claim by any third party with respect to the Company's technology. The term of these indemnification agreements is generally perpetual after execution of the agreement. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of its status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. To date, the Company has not incurred any losses or any material costs related to this indemnification obligation and no claims with respect thereto were outstanding. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations and cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2021 and 2020.

10. Convertible Preferred Stock

The Company has issued Series A, Series B, Series C-1, Series C-2, Series D, Series E and Series F convertible preferred stock (collectively, the "Convertible Preferred Stock"). The holders of Convertible Preferred Stock have liquidation rights in the event of a deemed liquidation that, in certain circumstances, is not solely within the control of the Company. Therefore, the Convertible Preferred Stock is classified outside of stockholders' deficit. The Company's certificate of incorporation, as amended and restated, authorized the Company to issue 78,112,639 and 70,832,388 shares of $0.00001 par value convertible preferred stock as of December 31, 2021 and 2020, respectively.

In March 2020 through July 2020, the Company issued a total of 12,838,573 shares of Series E convertible preferred stock (the "Series E Convertible Preferred Stock") at $4.2893 per share to investors for net proceeds of $54,373, net of issuance costs of $695.

In March 2020, contemporaneous with the Series E Convertible Preferred Stock financing, the shareholders of the Company approved a reduction in the authorized shares of Series D Convertible Preferred Stock by 1,641,778 shares to 11,994,461 shares.

In June 2021 through July 2021, the Company issued a total of 11,927,048 shares of Series F convertible preferred stock (the "Series F Convertible Preferred Stock") at $8.3843 per share to investors for net proceeds of $99,846, net of issuance costs of $154. The Series F Convertible Preferred Stock has the same rights and preferences as the Series A, Series B, Series C-1, Series C-2, Series D and Series E Convertible Preferred Stock.

In June 2021, contemporaneous with the Series F Convertible Preferred Stock financing, the shareholders of the Company approved a reduction of the authorized shares of Series E Convertible Preferred Stock by 4,646,797 shares to 12,838,573 shares.

As of each balance sheet date, Convertible Preferred Stock consisted of the following:

	December 31, 2021				
	Convertible Preferred Shares Authorized	Convertible Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A Convertible Preferred Stock	5,500,000	5,500,000	$ 6,510	$ 8,974	5,500,000
Series B Convertible Preferred Stock	11,451,453	11,332,970	15,459	21,939	11,332,970
Series C-1 Convertible Preferred Stock	9,064,640	9,064,640	20,114	29,216	9,064,640
Series C-2 Convertible Preferred Stock	15,336,464	15,336,464	47,129	64,561	15,336,464
Series D Convertible Preferred Stock	11,994,461	11,994,461	43,899	55,821	11,994,461
Series E Convertible Preferred Stock	12,838,573	12,838,573	54,373	60,917	12,838,573
Series F Convertible Preferred Stock	11,927,048	11,927,048	99,846	103,306	11,927,048
	78,112,639	77,994,156	$ 287,330	$ 344,734	77,994,156

	December 31, 2020				
	Convertible Preferred Shares Authorized	Convertible Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A Convertible Preferred Stock	5,500,000	5,500,000	$ 6,510	$ 8,644	5,500,000
Series B Convertible Preferred Stock	11,451,453	11,332,970	15,459	21,079	11,332,970
Series C-1 Convertible Preferred Stock	9,064,640	9,064,640	20,114	28,000	9,064,640
Series C-2 Convertible Preferred Stock	15,336,464	15,336,464	47,129	61,731	15,336,464
Series D Convertible Preferred Stock	11,994,461	11,994,461	43,899	53,182	11,994,461
Series E Convertible Preferred Stock	17,485,370	12,838,573	54,373	57,622	12,838,573
	70,832,388	66,067,108	$ 187,484	$ 230,258	66,067,108

In January 2014, the Company issued a fully vested warrant to purchase 118,483 shares of the Company's Series B Convertible Preferred Stock in connection with the 2014 Note (See Note 8).

The holders of the Convertible Preferred Stock have the following rights and preferences:

Voting

The holders of the Convertible Preferred Stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote and have the right to vote the number of shares equal to the number of shares of common stock into which such Convertible Preferred Stock could convert on the record date for determination of stockholders entitled to vote. In addition, holders of Series A, Series B, Series C-1, Series C-2, Series D, Series E and Series F convertible preferred stock, voting as a separate class, are entitled to elect four directors of the Company.

Dividends

The holders of Convertible Preferred Stock are entitled to receive cumulative dividends in preference to any dividend on common stock at the rate of 6.0% of the Original Issue Price (as defined below) per share, per annum. Dividends are payable only when, as, and if declared by the board of directors. No dividends have been declared or paid by the Company since its inception in August 2010. The Original Issue Price is $1.00 per share for Series A convertible preferred stock, $1.266 per share for Series B convertible preferred stock, $2.2356 per share for Series C-1 convertible preferred stock, $3.0756 per share for Series C-2 convertible preferred stock, $3.6667 per share for Series D convertible preferred stock, $4.2893 per share for Series E convertible preferred stock and $8.3843 per share for Series F convertible preferred stock subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to Convertible Preferred Stock.

Liquidation Preference

In the event of any liquidation, voluntary or involuntary, dissolution or winding up of the Company or Deemed Liquidation Event (as defined below), holders of the Convertible Preferred Stock are entitled to receive, in preference to all other stockholders, and to the extent available, an amount equal to the Original Issue Price per share, adjusted for any stock dividends, stock splits or reclassifications, plus any accruing dividends accrued but unpaid, whether or not declared, together with any other dividends declared but unpaid. In the event that proceeds are not sufficient to permit payment in full to these holders, the proceeds will be ratably distributed among the holders of the Convertible Preferred Stock on a *pari passu* basis to the full preferential amount each such holder is otherwise entitled to receive.

After payments have been made in full to the holders of the Convertible Preferred Stock, then, to the extent available, holders of the common stock will receive the remaining amounts available for distribution ratably in

proportion to the number of common shares held by them provided, however, if the holders of any series of the Convertible Preferred Stock would receive a greater amount of the proceeds if they had converted their shares of the Convertible Preferred Stock, then such holders shall not receive any proceeds under the preceding paragraph and will receive proceeds on an as converted to common stock basis.

Unless the holders of at least 60.0% of the then outstanding shares of the Convertible Preferred Stock, voting together as single class, elect otherwise, a Deemed Liquidation Event shall include a merger or consolidation (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

Conversion

Each share of Series A, Series B, Series C-1, Series C-2, Series D, Series E and Series F convertible preferred stock is convertible into common stock. Prior to authorization of the Series C-1 Convertible Preferred Stock, Series A Convertible Preferred Stock and Series B Convertible Preferred Stock was convertible into common stock, at the option of the stockholder at any time after the date of issuance. Upon authorization of the Series C-1 Convertible Preferred Stock, each class of the Convertible Preferred Stock is convertible into common stock, at the option of the stockholder, beginning two years after the effective issuance date, or August 2016. Each share of Series A, Series B, Series C-1, Series C-2, Series D, Series E and Series F convertible preferred stock will automatically be converted into shares of common stock, at the applicable conversion ratio of each series then in effect, (i) upon a qualified public offering, defined as the closing of a firm commitment underwritten public offering in which the gross proceeds raised equal or exceed $60,000; (ii) the consummation of a qualified SPAC transaction; or (iii) a date and time, or occurrence of an event specified by vote or written consent of 60.0% of the holders of the then outstanding shares of Convertible Preferred Stock.

The conversion ratio of each series of the Convertible Preferred Stock is determined by dividing the Original Issue Price of each series of convertible preferred stock by the Conversion Price of each series. The Conversion Price is $1.00 for Series A Convertible Preferred Stock, $1.266 for Series B Convertible Preferred Stock, $2.2356 for Series C-1 Convertible Preferred Stock, $3.0756 for Series C-2 Convertible Preferred Stock, $3.6667 for Series D Convertible Preferred Stock, $4.2893 per share for Series E Convertible Preferred Stock and $8.3843 per share for Series F Convertible Preferred Stock, resulting in a conversion ratio of 1-for-1 for each series of the Convertible Preferred Stock.

Redemption

Prior to August 19, 2014, the carrying values of the Series A Convertible Preferred Stock and Series B Convertible Preferred Stock were being accreted to their redemption values through March 8, 2018. Upon the closing of the Series C-1 convertible preferred stock financing, the redemption rights of the Series A Convertible Preferred Stock and Series B Convertible Preferred Stock were removed. As a result of the removal of the redemption rights, as of August 19, 2014, the Company ceased the periodic recording of adjustments to accrete the carrying values of Series A Convertible Preferred Stock and Series B Convertible Preferred Stock to each of their redemption values. None of the series of the Company's convertible preferred stock are redeemable as of December 31, 2021.

11. Common Stock

The Company's certificate of incorporation, as amended and restated, authorized the Company to issue 107,000,000 and 96,000,000 shares of $0.00001 par value common stock as of December 31, 2021 and 2020, respectively. The voting, dividend and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers and preferences of the holders of the Convertible Preferred Stock set forth above.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends whenever funds are legally available and when declared by the board of directors, subject to the prior rights of holders of all classes of stock outstanding. When dividends are declared on shares of common stock, the Company must declare at the same time a dividend payable to the holders of the Convertible Preferred Stock equivalent to the dividend amount they would receive if each preferred share were converted into common stock. The Company may not pay dividends to common stockholders until all dividends accrued or declared but unpaid on the Convertible Preferred Stock have been paid in full. No dividends have been declared to date.

As of December 31, 2021, the Company had 102,950,218 shares of common stock available for the conversion of outstanding shares of the Convertible Preferred Stock (See Note 10), the exercise of outstanding stock options and the number of shares remaining available for grant under the Company's 2011 Stock Incentive Plan (See Note 12) as well as the exercise of the warrant to purchase common stock (See Note 6) and Series B convertible preferred stock (See Note 8), assuming the warrant to purchase Series B convertible preferred stock became a warrant to purchase common stock at the applicable Series B convertible preferred stock conversion ratio.

12. Stock-Based Compensation

The Company's 2011 Stock Incentive Plan, as amended, (the "Plan") provides for the Company to sell or issue common stock or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, officers, directors, consultants and advisors of the Company. Incentive stock options may only be granted to employees. The Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the term of stock option may not be greater than ten years. The Company values its common stock by taking into consideration its most recently available valuation of common stock performed by an independent valuation analyst engaged by management and the board of directors, as well as additional factors which may have changed since the date of the most recently available valuation through the date of grant. The Company generally grants stock-based awards with service conditions only ("service-based" awards).

Stock options granted under the Plan generally vest over four years, with some options having a 25% vesting after one year and the balance vesting pro rata each month and others vesting pro rata each month. The Company also issues performance-based awards from time to time, which are expensed based on the number of options ultimately expected to vest.

The total number of shares of common stock that may be issued under the Plan was 25,740,000 and 22,740,000 as of December 31, 2021 and 2020, respectively, of which 4,131,844 and 2,433,612 were available for future grant as of December 31, 2021 and 2020, respectively.

Stock Option Valuation

The assumptions that the Company used to determine the fair value of stock options granted to employees and directors were as follows:

	Years Ended December 31,	
	2021	2020
Risk-free interest rate	0.9%—1.2%	0.4%—0.7%
Weighted average expected term (in years)	6.0	5.9
Weighted average expected volatility	59%	53%
Weighted average expected dividend yield	0%	0%
Fair value of common stock per share	$3.25	$1.81

Stock Options

The following table summarizes the Company's stock option activity since December 31, 2020:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2020	16,508,062	$ 1.30	6.5	$ 8,388
Grant	2,258,793	3.25		
Exercised	(71,456)	0.56		
Forfeited	(957,025)	2.03		
Outstanding at December 31, 2021	17,738,374	$ 1.51	5.9	$ 71,070
Options exercisable at December 31, 2021	13,641,669	$ 1.25	5.0	$ 58,293

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2021 and 2020 was $1.76 and $0.89 per share, respectively. The total intrinsic value of stock options exercised during the years ended December 31, 2021 and 2020 was $324 and $96, respectively.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The total fair value of stock options vested during the years ended December 31, 2021 and 2020 was $2,084 and $1,955 respectively.

Stock-Based Compensation Expense

The Company recorded stock-based compensation expense related to stock options in the following expense categories within its consolidated statements of operations and comprehensive loss:

	Year Ended December 31,	
	2021	2020
Research and development expenses	$ 1,034	$ 758
General and administrative expenses	1,057	868
	$ 2,091	$ 1,626

Total unrecognized stock-based compensation expense for all stock-based awards was $4,932 as of December 31, 2021, which is expected to be recognized over a weighted average period of 2.9 years.

13. Income Taxes

During the years ended December 31, 2021 and 2020, the Company recorded no income tax benefits for the net operating losses incurred in each year due to its uncertainty of realizing a benefit from those items. All of the Company's losses before income taxes were generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2021	2020
Federal statutory income tax rate	21.0%	21.0%
State income taxes, net of federal benefit	4.8	5.8
Research and development tax credits	3.9	4.9
Permanent differences	(0.6)	(1.1)
Change in valuation allowance	(29.1)	(30.6)
Effective income tax rate	— %	— %

Net deferred tax assets as of December 31, 2021 and 2020 consisted of the following:

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 53,593	$ 44,554
Research and development tax credit carryforwards	8,616	7,092
Deferred rent	—	355
Lease liabilities	349	—
Stock-based compensation expense	1,827	1,539
Accrued expenses and other	409	293
Capitalized patent and trademark costs	1,056	920
Other	240	20
Total deferred tax assets	66,090	54,773
Deferred tax liabilities:		
Right-of-use lease assets	(169)	—
Other	(83)	(194)
Valuation allowance	(65,838)	(54,579)
Net deferred tax assets	$ —	$ —

As of December 31, 2021, the Company had federal and state net operating loss carryforwards of $198,906 and $194,595, respectively, which may be available to reduce future taxable income and begin to expire at various dates beginning in 2030 for federal and state purposes. As of December 31, 2021, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $6,478 and $2,706, respectively, which begin to expire in 2031 and 2027, respectively.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company has not currently completed an evaluation of ownership changes through December 31, 2021 to assess whether utilization of the Company's net operating loss or research and development credit carryforwards would be subject to an annual limitation under Section 382. To the extent an ownership change occurs in the future, the net operating loss and credit carryforwards may be subject to limitation. Further, until a study is completed and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has not yet conducted a study of its research and development credit carryforwards. This study may result in an increase or decrease to the Company's credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A valuation allowance has been provided against the Company's credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. As a result, there would be no impact to the consolidated statements of operations and comprehensive loss or consolidated statements of cash flows if an adjustment were required.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets, which are comprised principally of net operating losses and research and development tax credit carryforwards. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of

the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2021 and 2020, respectively. Management reevaluates the positive and negative evidence at each reporting period.

Changes in the valuation allowance for deferred tax assets during the year ended December 31, 2021 and 2020 related primarily to the increase in federal and state net operating loss carryforwards and available research and development credits and were as follows:

	Year Ended December 31,	
	2021	2020
Valuation allowance at beginning of year	$ 54,579	$ 45,244
Increases recorded to income tax provision	11,259	9,335
Valuation allowance at end of year	$ 65,838	$ 54,579

The Company's policy is to recognize interest and penalties for uncertain tax position as a component of income tax expense. The Company has not recorded any amounts for unrecognized tax benefits, interest, or penalties historically through December 31, 2021.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security (CARES) Act was signed into law. The Act contains several new or changed income tax provisions, including but not limited to the following: increased limitation threshold for determining deductible interest expense and the ability to carry back net operating losses incurred from tax years 2018 through 2021 up to the five preceding tax years. The Company has evaluated the new tax provisions of the CARES Act and determined the impact to be either immaterial or not applicable.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company's tax returns are still open under statute from 2018 to the present, however carryforward attributes that were generated prior to January 1, 2018 may still be adjusted upon examination by federal or state tax authorities if they have been or will be utilized in a future period.

14. 401(k) Savings Plan

The Company maintains a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all U.S. employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax and or after-tax basis. Company contributions to the plan may be made at the discretion of the Board of Directors. The Company has not made any matching or discretionary contributions to date under the 401(k) savings plan.

15. Reduction in Force

In April 2020, the Company announced the reduction of the size of its workforce by 15 employees or approximately 25% of its headcount, most of which was completed in the second quarter of 2020. In 2020, the Company incurred $188 in severance costs for the impacted employees, of which $92 was recorded in research and development expenses and $96 was recorded in general and administrative expenses. No severance costs were incurred in 2021 related to such reduction in force event.

16. Related Party Transactions

A consultant to the Company, who was appointed to the Company's Board of Directors in 2018, resigned from the Board in June 2020. During the time he served as a member of the Company's Board of Directors in 2020, the Company paid him consulting fees of approximately $13.

17. Net Loss Per Share

The following securities that could potentially dilute basic net loss per share in the future were not included in the computation of diluted net loss per share for the periods presented, because to do so would have been antidilutive:

	Year Ended December 31,	
	2021	2020
Series A Convertible Preferred Stock	5,500,000	5,500,000
Series B Convertible Preferred Stock	11,332,970	11,332,970
Series C-1 Convertible Preferred Stock	9,064,640	9,064,640
Series C-2 Convertible Preferred Stock	15,336,464	15,336,464
Series D Convertible Preferred Stock	11,994,461	11,994,461
Series E Convertible Preferred Stock	12,838,573	12,838,573
Series F Convertible Preferred Stock	11,927,048	—
Outstanding stock options	17,738,374	16,508,062
Common stock warrants	346,832	346,832
Series B Convertible Preferred Stock warrants	118,483	118,483
Total	96,197,845	83,040,485

18. Subsequent Events

The Company has evaluated subsequent events and transactions through April 4, 2022, the date these consolidated financial statements were available to be issued, for potential recognition or disclosure in the consolidated financial statements. Except as described below, the Company has concluded that no additional subsequent events have occurred that require disclosure.

In January 2022, the Company fully paid off the 2019 Note by making a lump-sum payment to the lender of the Term Loans for a total amount of $16,130. See Note 6.

In January 2022, the Company sold and issued $20,075 aggregate principal amount of convertible promissory notes (the “2022 Notes”) in a private placement transaction. The 2022 Notes accrue interest at a rate of 3.0% per annum and mature on July 11, 2023 (the “Maturity Date”), if not previously converted to common stock or preferred stock or repaid in cash prior to the Maturity Date. The company is currently evaluating the terms of the 2022 Notes and the related accounting considerations, which includes an evaluation of any potential embedded features.

Through and including , 2022 (the 25th day after the date of this prospectus), all dealers effecting transactions in the common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

Shares

Common Stock

PROSPECTUS

BofA Securities

Morgan Stanley

Evercore ISI

, 2022

Part II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the Nasdaq listing fee.

	Amount
SEC registration fee	$ *
FINRA filing fee	*
Nasdaq listing fee	*
Accountants' fees and expenses	*
Legal fees and expenses	*
Transfer agent's fees and expenses	*
Printing and engraving expenses	*
Miscellaneous expenses	*
Total	**$ ***

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

Fractyl Health, Inc. is incorporated under the laws of the State of Delaware. Reference is made to Section 102(b)(7) of the DGCL, which enables a corporation in its original certificate of incorporation or an amendment thereto to eliminate or limit the personal liability of a director for violations of the director's fiduciary duty, except (1) for any breach of the director's duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) pursuant to Section 174 of the DGCL, which provides for liability of directors for unlawful payments of dividends or unlawful stock purchase or redemptions or (4) for any transaction from which the director derived an improper personal benefit.

Section 145(a) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses

(including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, he or she is fairly and reasonably entitled to indemnity for such expenses which the adjudicating court shall deem proper.

Section 145(g) of the DGCL provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the DGCL.

We expect that the amended and restated certificate of incorporation adopted by us prior to the completion of this offering will provide that no director of our company shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, except for liability (1) for any breach of the director's duty of loyalty to us or our stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) in respect of unlawful dividend payments or stock redemptions or repurchases or other distributions pursuant to Section 174 of the DGCL, or (4) for any transaction from which the director derived an improper personal benefit. In addition, our charter will provide that if the DGCL is amended to authorize the further elimination or limitation of the liability of directors, then the liability of a director of our company shall be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

We also expect our charter will further provide that any amendment, repeal or modification of such article unless otherwise required by law will not adversely affect any right or protection existing at the time of such repeal or modification with respect to any acts or omissions occurring before such repeal or amendment of a director serving at the time of such repeal or modification.

We expect that our amended and restated certificate of incorporation adopted by us prior to the completion of this offering, will provide that we shall indemnify each of our directors and executive officers, and shall have power to indemnify our other officers, employees and agents, to the fullest extent permitted by the DGCL as the same may be amended (except that in the case of an amendment, only to the extent that the amendment permits us to provide broader indemnification rights than the DGCL permitted us to provide prior to such the amendment) against any and all expenses, judgments, penalties, fines and amounts reasonably paid in settlement that are incurred by the director, officer or such employee or on the director's, officer's or employee's behalf in connection with any threatened, pending or completed proceeding or any claim, issue or matter therein, to which he or she is or is threatened to be made a party because he or she is or was serving as a director, officer or employee of our company, or at our request as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of our company and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. We expect the amended and restated certificate of incorporation will further provide for the advancement of expenses to each of our directors and, in the discretion of the board of directors, to certain officers and employees, in advance of the final disposition of such action, suit or proceeding only upon receipt of an undertaking by such person to repay all amounts advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal that such person is not entitled to be indemnified for such expenses.

In addition, we expect the amended and restated certificate of incorporation will provide that the right of each of our directors and officers to indemnification and advancement of expenses shall not be exclusive of any

other right now possessed or hereafter acquired under any statute, provision of the charter or bylaws, agreement, vote of stockholders or otherwise. Furthermore, our amended and restated certificate of incorporation will authorize us to provide insurance for our directors, officers, employees and agents against any liability, whether or not we would have the power to indemnify such person against such liability under the DGCL or the bylaws.

We intend to enter into indemnification agreements with each of our directors and our executive officers. These agreements will provide that we will indemnify each of our directors and such officers to the fullest extent permitted by law and our amended and restated certificate of incorporation.

We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of our company arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we will enter into in connection with the sale of the common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act, against certain liabilities.

Item 15. Recent Sales of Unregistered Securities.

During the past three years, we issued securities that were not registered under the Securities Act as set forth below. The following is a summary of transactions during the preceding three fiscal years involving sales of our securities that were not registered under the Securities Act:

(a) Issuance of Capital Stock

From March to July 2020, we issued and sold to investors in a private placement an aggregate of 12,729,465 shares of Series E Preferred Stock at a purchase price of $4.2893 per share, for aggregate consideration of approximately $54.6 million.

In June and July 2021, we issued and sold to investors in a private placement an aggregate of 11,927,048 shares of Series F Preferred Stock at a purchase price of $8.3843 per share, for aggregate consideration of approximately $100.0 million.

In January 2022, we entered into a note purchase agreement with certain individual and institutional accredited investors, pursuant to which we sold and issued approximately $20.1 million aggregate principal amount of convertible promissory notes in exchange for aggregate cash proceeds of approximately $20.1 million.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 15 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The recipients of securities in the transactions described above represented that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions.

(b) Stock Option Grants and Option Exercises

Since January 1, 2019 through the date of this prospectus, we granted to our employees, officers, directors, consultants and advisors options to purchase up to 9,767,929 shares of our common stock under the 2011 Plan, at a weighted average exercise price of $2.48 per share. 1,517,314 of these options were terminated, expired without being exercised or were otherwise forfeited.

No underwriters were involved in the foregoing issuances of securities. The issuances of stock options described in this paragraph (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors, consultants and advisors, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statements.

Exhibit No.	Description of Exhibit
1.1*	Form of Underwriting Agreement.
3.1**	Amended and Restated Certificate of Incorporation of the Registrant (as amended and currently in effect).
3.2**	Bylaws of the Registrant (currently in effect).
3.3*	Form of Amended and Restated Certificate of Incorporation of the Registrant (to be in effect upon the consummation of this offering).
3.4*	Form of Amended and Restated Bylaws of the Registrant (to be in effect upon the consummation of this offering).
4.1**	Specimen Stock Certificate evidencing the shares of common stock.
4.2**	Fifth Amended and Restated Investors' Rights Agreement, dated June 9, 2021, by and among the Registrant and certain of its stockholders.
5.1*	Opinion of Latham & Watkins LLP.
10.1†**	Fractyl Health, Inc. Amended and Restated 2011 Stock Incentive Plan and forms of award agreements thereunder.
10.2†*	Employment Letter Agreement, dated , by and between the Registrant and Harith Rajagopalan, M.D., Ph.D.
10.3†*	Employment Letter Agreement, dated , by and between the Registrant and Lisa A. Davidson.
10.4†*	Employment Letter Agreement, dated , by and between the Registrant and Jay D. Caplan.
10.5†*	Employment Letter Agreement, dated , by and between the Registrant and Juan Carlos Lopez-Talavera, M.D., Ph.D.
10.6**	Lease Agreement, dated November 17, 2015, by and between the Registrant (f/k/a Fractyl Laboratories, Inc.) and BP 17 Hartwell LLC.
10.7†*	Fractyl Health, Inc. 2022 Incentive Award Plan and forms of award agreements thereunder.
10.8†*	Fractyl Health, Inc. 2022 Employee Stock Purchase Plan.
10.9†*	Fractyl Health, Inc. Non-Employee Director Compensation Program.
10.10†**	Form of Indemnification Agreement by and among the Registrant and its directors and officers.
21.1**	List of Subsidiaries of the Registrant.
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm.
23.2*	Consent of Latham & Watkins LLP (included in Exhibit 5.1).
24.1*	Power of Attorney (included on signature page).
107*	Filing Fee Table.

* To be filed by amendment.

** Previously filed.

† Indicates a management contract or compensatory plan or arrangement.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriter, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Lexington, Commonwealth of Massachusetts, on this day of , 2022.

FRACTYL HEALTH, INC.

By: _____

Harith Rajagopalan, M.D., Ph.D.
Co-Founder, Chief Executive Officer and Director

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Fractyl Health, Inc., hereby severally constitute and appoint Harith Rajagopalan and Lisa A. Davidson, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities held on the dates indicated.

Signature	Title	Date
Harith Rajagopalan, M.D., Ph.D.	Co-Founder, Chief Executive Officer and Director (Principal Executive Officer)	, 2022
Lisa A. Davidson	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	, 2022
Kelly Barnes	Director	, 2022
William W. Bradley	Director	, 2022
Brian Dovey	Director	, 2022
Marc Elia	Director	, 2022
Clive Meanwell, M.B., Ch.B., M.D.	Director	, 2022
Ajay Royan	Director	, 2022
Amy W. Schulman	Director	, 2022
Allan R. Will	Chairman	, 2022