



2025

Annual Report

Dear Stockholders,

A year ago, we entered 2025 with three clear commitments: deliver data readouts for Revita® in weight maintenance, advance the commercial and regulatory foundation for Revita, and submit Clinical Trial Applications for our Rejuva® gene therapy candidate, RJVA-001, in type 2 diabetes. I am pleased to announce we have delivered on all three commitments.

The GLP-1 revolution has transformed obesity treatment, but also revealed a defining unmet need: the majority of patients who discontinue these medications regain two-thirds or more of their lost weight within a year. Millions are expected to discontinue annually, creating a large and growing unmet need for post-GLP-1 weight maintenance. Fractyl Health stands alone developing the first potential procedural option for drug-free, durable post-GLP-1 weight maintenance.

Revita: REMAIN-1, Our Pivotal Study

REMAIN-1, a randomized, double-blind, sham-controlled study in patients who have discontinued GLP-1 therapy, successfully completed randomization in February 2026, with topline six-month primary endpoint data anticipated in early Q4 2026.

Interim Midpoint Cohort data were compelling. Six-month randomized data announced in Q1 2026 showed a statistically significant correlation between duodenal ablation length and weight maintenance. In participants with above-median GLP-1-induced weight loss who received greater than 14 cm of ablation, Revita participants retained 88% of their GLP-1-induced weight loss at six months versus 60% in sham. No Revita-related serious adverse events have been observed to date. In March 2026, we received favorable FDA feedback on our De Novo classification request and anticipate submitting a potential De Novo marketing application in late Q4 2026.

Rejuva: Pioneering Metabolic Gene Therapy

While Revita represents our near-term commercial opportunity, Rejuva represents the next frontier: durable, potentially curative metabolic interventions through a single administration. We submitted Clinical Trial Applications for RJVA-001, our lead T2D candidate, to regulators in the EU and Australia in H2 2025. Subject to authorization, we plan to dose first patients and expect reporting preliminary data in H2 2026. RJVA-002, our dual GIP/GLP-1 obesity candidate, has generated striking preclinical results.

Financial Position and Disciplined Stewardship

We ended 2025 with \$81.5 million in cash and cash equivalents, with runway into early 2027. This funds execution through anticipated REMAIN-1 Pivotal topline data in early Q4 2026 and the potential De Novo marketing application submission in late Q4 2026.

2026: A Year of Catalysts

We anticipate significant milestones ahead, making 2026 a transformative year for Fractyl Health:

Revita

Q2 2026:

1-year REVEAL-1 Cohort data

Q3 2026:

1-year REMAIN-1 Midpoint Cohort randomized data

Early Q4 2026:

Topline 6-month randomized data from REMAIN-1 Pivotal Cohort

Late Q4 2026:

Potential FDA De Novo marketing application submission in post-GLP-1 weight maintenance

Rejuva

Q2 2026:

Regulatory feedback on CTAs for RJVA-001

H2 2026:

First-in-human dosing of RJVA-001, subject to CTA authorization, and expected reporting of preliminary data

Our Vision: Beyond Chronic Management

We founded Fractyl Health on the belief that metabolic disease could be treated at its root cause, not merely managed. What patients want most is freedom from lifelong disease management and a genuine path to resolution. Positive pivotal data for Revita would establish the first proven therapy for post-GLP-1 weight maintenance; and first-in-human data for RJVA-001 holds promise for a durable metabolic reset from a single treatment. Together, these represent the most consequential inflection points in Fractyl Health's history for patients, science, and our stockholders.

I am deeply grateful for your continued support and confidence.

Sincerely,



Harith Rajagopalan, M.D., Ph.D.
Co-Founder and Chief Executive Officer
Fractyl Health, Inc.



**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2025

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission File Number: 001-41942

Fractyl Health, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

3 Van de Graaff Drive, Suite 200
Burlington, MA
(Address of principal executive offices)

27-3553477
(I.R.S. Employer
Identification No.)

01803
(Zip Code)

Registrant's telephone number, including area code: (781) 902-8800

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	(Name of each exchange on which registered)
Common Stock, \$0.00001 par value per share	GUTS	The Nasdaq Global Market

Securities registered pursuant to section 12(g) of the Act:

None
(Title of class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. YES NO

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). YES NO

The aggregate market value of the voting and non-voting common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on The Nasdaq Global Market on June 30, 2025, was \$49.6 million. Solely for purposes of this disclosure, shares of common stock held by executive officers, directors and certain stockholders of the registrant as of such date have been excluded because such holders may be deemed to be affiliates.

As of March 1, 2026, the number of shares of the registrant's common stock outstanding was 158,648,963.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the registrant's 2026 annual meeting of shareholders, which is to be filed within 120 days after the end of the registrant's fiscal year ended December 31, 2025 are incorporated by reference into Part III of this Form 10-K, to the extent described in Part III.

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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 subsidiaries.

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 (“U.S. GAAP”). Our fiscal year ends on December 31 of each year. References to 2025 and 2024 refer to the year ended December 31, 2025 and the year ended December 31, 2024, respectively. Our most recent fiscal year ended on December 31, 2025.

Certain monetary amounts, percentages and other figures included in this Annual Report on Form 10-K have been subject to rounding adjustments. Percentage amounts included in this Annual Report on Form 10-K 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 Annual Report on Form 10-K may vary from those obtained by performing the same calculations using the figures in our consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Certain other amounts that appear in this Annual Report on Form 10-K may not sum due to rounding.

TRADEMARKS AND TRADENAMES

This Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 believed 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 Part I, Item 1A. *Risk Factors*. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent third parties and by us.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that can involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy (including our Strategic Reprioritization, as defined herein), prospective products, or product candidates, plans regarding or status of clinical trials or studies and their design, our plans for readouts of interim or final results, product approvals, communications with or submissions to the U.S. Food and Drug Administration (the “FDA”), 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, the anticipated use of or impact of the net proceeds from the ATM Offering, the August 2025 Offering and the September 2025 Offering, and the timing of any of the foregoing 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 Annual Report on Form 10-K 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, certifications and approvals, including final regulatory authorizations, approval certifications 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 authorized, approved, certified 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 authorized, 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;
- the status, breadth and strength of our intellectual property portfolio and its ability to protect our innovations;
- our ability to obtain patent coverage for our products;

- our ability to successfully defend litigation and other similar complaints and to establish and maintain intellectual property rights covering our products;
- developments and projections relating to our competitors and our industry;
- our expectations related to the use of proceeds from our financing activities;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- 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 adverse macroeconomic conditions, geopolitical events 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 Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described in Part I, Item 1A. *Risk Factors* and elsewhere in this Annual Report on Form 10-K. 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, 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 Annual Report on Form 10-K, 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.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. *Risk Factors*. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business 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 (“U.S.”), 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, we expect to continue to incur significant net losses for the foreseeable future and may never achieve or sustain profitability, and we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern;
- We require substantial additional capital or must implement other business strategies to execute our operating plan and continue to operate as a going concern. 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 clearance and certification processes of the U.S. Food and Drug Administration (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;
- 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;
- We currently conduct and may in the future conduct clinical studies for our product candidates outside the U.S., and the FDA or comparable foreign regulatory authorities may not accept data from such studies;
- We may not be able to submit investigational device exemptions (“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;
- We may experience delays, interruptions or additional costs in obtaining and maintaining government regulatory approvals, licenses, certifications or reimbursements as a result of federal government shutdowns, reduced staffing or funding lapses. Such delays or disruptions could adversely affect our ability to develop, commercialize or market our product candidates, or to receive payments or reimbursements in a timely manner;
- We may not be able to submit investigational new drug applications (“INDs”) or IND amendments with the FDA, clinical trial applications (“CTAs”) or comparable documents with regulatory bodies in foreign jurisdictions to commence additional clinical studies on the timelines we expect, and even if we are able to, the FDA or other comparable foreign regulatory authorities may not permit us to proceed;
- We are substantially dependent on the success of our lead product candidate, Revita[®], and our lead gene therapy product candidate, RJVA-001, in the Rejuva[®] platform. If we are unable to obtain marketing authorization or certification for and commercialize any of our current or future product candidates in a timely manner, our business will be harmed;
- 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;

- Additional time may be required to develop and obtain regulatory approval or certification for our Rejuva gene therapy candidates because we expect them to be regulated as a combination product;
- We cannot be certain that our Rejuva gene therapy candidates will successfully complete preclinical and clinical studies, or that they will not cause significant adverse events or toxicities. There can be no assurance that any development problems we experience in the future related to our Rejuva gene therapy candidates or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved;
- 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 candidates 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. 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 clinical utility and commercial adoption of the device;
- We have never obtained marketing authorization for a product candidate in the U.S. and we may be unable to obtain, or may be delayed in obtaining, marketing authorization for any product candidate in the U.S.;
- We substantially rely, and expect to continue to rely, on third parties, including independent clinical investigators and contract research organizations (“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;
- 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;
- We contract with third parties for the manufacture and supply 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;
- If we or our suppliers fail to comply with the FDA’s quality system and/or good manufacturing practice regulations, this could impair our ability to market our products in a cost-effective and timely manner;
- 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;
- 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; and
- 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 marketing authorization.

PART I

Item 1. Business.

Our Company

We are a clinical stage metabolic therapeutics company focused on pioneering novel approaches to treat obesity and type 2 diabetes (“T2D”). Our Revita[®] and Rejuva[®] candidates are designed to target root causes of metabolic diseases, allowing us to advance metabolic disease treatment from chronic management towards prevention and reversion of the disease.

Despite advances in treatment over the last 50 years, obesity and T2D continue to be principal and rapidly growing drivers of morbidity and mortality. According to the Centers for Disease Control approximately 115 million people in the U.S. have prediabetes and/or are living with obesity, and an additional approximately 27 million people have T2D and are potentially on medical therapy. Within the past two years, the unmet need in obesity has shifted rapidly from identifying treatments that can achieve short-term weight loss to identifying treatments that can enable durable weight maintenance. While highly potent drugs in the glucagon-like peptide-1 receptor agonist (“GLP-1RA”) class are now available to lower weight and blood sugar, these agents have high discontinuation rates that lead to a substantial risk of weight and metabolic rebound. According to a Kaiser Family Foundation Health Tracking Poll from November 2025, approximately 12% of adults are taking glucagon-like peptide-1 (“GLP-1”) drugs (an increase of 6 percentage points from May 2024), translating to approximately 30 million patients potentially on therapies that require chronic administration and do not correct the underlying disease of obesity. Despite the growing interest in these drugs, a Blue Health Intelligence brief from 2024 found that over 50% of patients discontinue GLP-1 drugs within three months of starting, long before patients can experience clinical benefit from these agents. Discontinuation of these agents typically leads to an immediate loss of metabolic benefit and weight rebound, as seen in Eli Lilly’s SURMOUNT-4 study with tirzepatide and Novo Nordisk’s STEP-1 extension study with semaglutide. For example, studies published in JAMA in 2023 found that patients lost approximately 20% of their body weight over 36 weeks while on tirzepatide. However, when patients discontinued the drug, they experienced approximately 14% weight regain in 52 weeks, approximately 5% of which was regained in the first three months after discontinuation. These high rates of drug discontinuation and weight regain demonstrate the need for new approaches that can enable durable maintenance of weight and metabolic health without requiring daily or weekly pharmacotherapy.

The Revita DMR System (“Revita”), our lead product candidate, is based on our insights surrounding the potential role of the gut in obesity. Revita is designed to remodel the duodenal lining via hydrothermal ablation (i.e. duodenal mucosal resurfacing) to reverse damage to intestinal nutrient sensing and signaling mechanisms caused by chronic high-fat and high-sugar diets that are a root cause of metabolic disease. Revita has U.S. FDA Breakthrough Device designation in weight maintenance for people with obesity who discontinue GLP-1 based therapy. We have received favorable FDA feedback on our De Novo classification request for Revita and anticipate submitting a potential De Novo marketing application in the late fourth quarter of 2026. We are evaluating Revita in the REMAIN-1 weight maintenance program, which is designed to evaluate Revita’s potential to maintain weight loss following GLP-1 based therapy discontinuation. The REMAIN-1 study includes three distinct participant cohorts that are conducted under a single IDE: the REVEAL-1 Cohort, the REMAIN-1 Midpoint Cohort and the REMAIN-1 Pivotal Cohort, which are designed to collectively establish the clinical and regulatory foundation for Revita in weight maintenance.

- The REVEAL-1 Cohort (n=22) is an open-label study in individuals with obesity who have lost at least 15% of their total body weight on a GLP-1 medication and who either need or choose to discontinue GLP-1 based therapy.
- The REMAIN-1 Midpoint Cohort (n=45) is a randomized, double-blind, sham-controlled pilot study to assess the potential of Revita to maintain weight loss after GLP-1 based therapy discontinuation.
- The REMAIN-1 Pivotal Cohort (n=315) is a randomized, double-blind, sham-controlled pivotal study to evaluate the safety and efficacy of Revita in maintaining weight loss.

The REMAIN-1 study was initiated in the third quarter of 2024. Enrollment of all three cohorts is complete and the REMAIN-1 Midpoint Cohort and REMAIN-1 Pivotal Cohort are fully randomized, as described further under “Ongoing REMAIN-1 Clinical Study” below.

We are also developing Rejuva, our novel and locally administered, adeno-associated virus (“AAV”)-delivered pancreatic gene therapy platform. Rejuva is designed to enable long-term remission of T2D and obesity by durably reprogramming

pancreatic islet cells to endogenously produce metabolic hormones. Rejuva leverages advanced delivery systems and proprietary screening methods to identify and develop metabolically active gene therapy candidates targeting the pancreas.

Our lead candidate from the Rejuva platform, RJVA-001, is designed to be delivered to the pancreas via a single endoscopic intervention to enable pancreatic beta cells to express GLP-1 locally via nutrient-responsive control. This gene therapy approach enables physiologic GLP-1 secretion without the high circulating levels that contribute to side effects seen with systemic GLP-based drugs.

Our second candidate from the Rejuva platform, RJVA-002, is a dual GIP/GLP-1 gene therapy and is currently in preclinical development. RJVA-002 expands the Rejuva platform into obesity, targeting dual incretin biology with the goal of achieving durable, well-tolerated, weight loss from a single intervention.

Additional information regarding the Rejuva platform is described under “Rejuva Platform Description” and “Preclinical Data Overview: Rejuva Gene Therapy Platform” below.

We believe Revita and Rejuva have the potential to revolutionize treatment across the spectrum of obesity and T2D, align the clinical and economic interests of key stakeholders around the long-term regression of metabolic disease, and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

Our Development Pipeline

Our development pipeline for Revita and Rejuva pancreatic gene therapy (“PGTx”) candidates target large market indications in obesity and T2D and aim to transform treatment from chronic symptom management to disease-modifying therapies that target the organ-level root causes of metabolic disease.

The following table summarizes our development pipeline and potential clinical opportunities across the spectrum of metabolic disease, from obesity (with or without prediabetes) to advanced T2D.

Revita <i>Outpatient endoscopic procedural therapy</i>			2026 Key Anticipated Milestones ¹		
Indication	Program	Recent accomplishments	Q2	Q3	Q4
Weight Maintenance	REVEAL-1 Cohort (Open Label)	✓ Durable 6-mo data shared (Dec '25)	1-year data		
	REMAIN-1 Midpoint Cohort	✓ Positive 6-month randomized data (Jan '26)		1-year data	
	REMAIN-1 Pivotal Cohort	✓ Completed randomization (Feb '26)			Topline 6-mo randomized data & potential De Novo marketing application submission

Rejuva <i>Local AAV-delivered pancreatic GLP-1 gene therapy</i>				2026 Key Anticipated Milestones ¹	
Indication	Program	Research	Lead selection	IND/CTA enabling	Phase 1
Type 2 Diabetes	RJVA-001	CTAs submitted			
Obesity	RJVA-002	Candidate nominated			

¹These forward-looking statements are based on management's current estimates and expectations. Refer to the latest disclosures filed with the SEC for a discussion regarding Risk Factors to these and other estimates and expectations. Abbreviations: CTA, clinical trial application, FIH, first-in-human.

What Sets Us Apart

Our vision is to develop transformative therapies that can prevent and eliminate metabolic disease. We plan to achieve this by creating disease-modifying therapies targeting the gut and pancreas, driving broad adoption of our innovative approach and improving real-world outcomes for patients and health systems. Our vision is supported by the following strengths:

Pioneering New Approaches Based on Deep Understanding of Metabolic Diseases

We are pioneering the development of disease-modifying therapies targeting the organ level root cause of metabolic disease. Our approach builds on over a decade of our research and the accumulation of independently published, supportive preclinical and clinical evidence, all implicating the gut and pancreas as validated, untapped targets in obesity and T2D. We

aim to restore and preserve the health of the key organs required for metabolic fitness and reduce the burden of metabolic disease for patients.

Developing Disease-Modifying Therapies that Provide Long-Term Metabolic Benefits and the Potential to Shift the Treatment Paradigm in Obesity and T2D

Our Revita and Rejuva programs are designed to target dysfunction in the duodenum and pancreas, respectively, to provide long-term metabolic benefits from a single administration. For this reason, we believe Revita and Rejuva offer the potential to address metabolic diseases in ways we believe current therapies do not, including the prevention and remission of the diseases. Specifically, Revita has the potential to support long-term, durable weight maintenance, while Rejuva offers the potential to drive T2D remission and achieve durable weight loss.

Rigorous Approach to Clinical Development

The Revita clinical program is designed to advance the development of Revita as a foundational outpatient procedural therapy for obesity. By targeting duodenal dysfunction, Revita aims to provide durable weight maintenance solutions, addressing a critical gap in current long-term obesity care. To date, we have evaluated Revita in over 500 participants across multiple clinical studies at sites in South America, Europe and the U.S., with favorable safety and tolerability, glycemic control and weight maintenance data. Our Rejuva platform with GLP-1 PGTx candidates has been evaluated in small and large animal models, as well as *ex vivo* murine and human islets. In preclinical head-to-head studies, Rejuva gene therapy candidates demonstrated weight reduction in a disease-relevant diet-induced obesity (“DIO”) mouse model, along with improvement in glycemic control and delayed T2D progression in a disease-relevant *db/db* mouse model compared to chronic administrations of semaglutide (the active agent in Ozempic and Wegovy). We are leveraging our extensive clinical therapeutic endoscopy experience with Revita to inform our clinical plans with our RJVA-001 and RJVA-002 T2D and obesity candidates, respectively. We believe our clinical and preclinical programs are supported by a robust intellectual property position, including issued patents and pending applications, intended to protect core elements of our technology and assets and provide meaningful barriers to entry.

Aligning Interests of Key Stakeholders: Patients, Referring Physicians, Providers, and Payors

We believe Revita and Rejuva, if approved, have the potential to offer clinical and economic benefits while reducing the burden of disease management compared to the current standard of care in obesity and T2D. We believe both programs have the potential to broadly align interests across key stakeholders involved in the treatment of obesity and T2D, and may have the following benefits to these groups:

- *Patients.* Improving weight loss maintenance and glycemic control, while reducing the number and burden of therapies required to adequately manage obesity and T2D.
- *Referring Physicians.* Preventing weight gain and lowering HbA1c for specific patient populations with a procedural therapy that reduces the workload in disease management and improves quality metrics associated with the disease.
- *Providers.* Straightforward, easy to train outpatient procedures, 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, potentially profitable service line for hospitals with a patient-friendly therapeutic option for a significant portion of their patients.
- *Payors.* Significant health economic benefits for payors who are currently struggling with the increasing expenses of obesity and T2D, driven primarily by unchecked disease progression and the lack of disease-modifying therapies.

Purpose-Built Leadership Team with Shared Mission to Advance Patient Care in Metabolic Disease

Our diverse leadership team, combining product development know-how, therapeutic expertise and commercial readiness, has over 150 years of collective experience in therapeutic development. We are mission-driven to develop novel disease-

modifying 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, weight maintenance, endocrine signaling, endoscopy and gene therapy.

Growth Strategies

Our mission is to develop transformative therapies that prevent and eliminate metabolic disease. To achieve this goal, we plan to employ the following strategies:

Establish Practice-Changing Levels of Evidence for Revita Across the Spectrum of Obesity

Our stepwise approach to regulatory marketing authorization will initially focus on patients with the highest unmet need in obesity, those who need to maintain weight loss after GLP-1 medication discontinuation and then progress to other unmet needs in the treatment and prevention of metabolic diseases, including T2D.

We believe our Revita clinical program, including our ongoing REMAIN-1 study, will provide comprehensive clinical evidence to support the potential of Revita as an investigational, potential disease-modifying procedural therapy for weight maintenance in obesity.

Rejuva Gene Therapy Platform to Enable Long-Term Remission of T2D and Obesity

To further our core strategy to treat and significantly reduce the burden of T2D and obesity, we are developing the Rejuva gene therapy platform, which is designed to enable long-term remission of T2D and obesity by durably reprogramming pancreatic islet cells to endogenously produce metabolic hormones. Based on this mechanism, we believe Rejuva could be a potentially first-in-class, nutrient-responsive (“smart”), gene therapy that durably improves metabolic control. Our platform utilizes a novel investigational pancreatic delivery device to administer gene therapy candidates directly to the pancreas (body and tail). We believe that our approach allows for the precise mechanical and molecular confinement of targeted, low dose gene therapy medicines that can address many of the challenges that limit the use of gene therapy in the pancreas and systemic GLP-1-based drugs today.

Execute Targeted and Efficient Go-to-Market Strategy for Revita

If Revita is approved in the U.S. for a weight maintenance indication, 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 learning and insights from the Revita clinical program and from the commercial pilot in Germany, we plan to assemble a targeted sales force initially focusing on a center of excellence model, working closely with gastrointestinal (“GI”) endoscopist “early adopters,” with a dedicated interest in bariatric and metabolic endoscopy. In parallel, we plan to leverage our letter of intent (“LOI”) with Everself (formerly Bariendo) as this potential partnership will bring a scalable, physician-driven platform designed to deliver metabolic endoscopic solutions at the nation’s largest network of high-volume hospital and ambulatory endoscopy centers across the U.S. We intend to roll out a robust procedural training and support program for GI endoscopists, which we believe will ensure seamless integration into their workflow and practice. We will also work with CMS and private insurers to seek to establish coverage and reimbursement for procedures using our Revita product candidate, a key strategy to support the commercial viability of Revita with providers.

Broaden the Indication and Use of Revita

If Revita is approved for a weight maintenance indication in the U.S., we plan to leverage our platform, technology, core capabilities and the data gathered from our prior clinical studies and the Revita clinical program to expand the indication and use of Revita within other unmet needs in the treatment and prevention of other serious metabolic diseases, including T2D.

Because of our broadly accessible and disease-modifying approach, we intend to make Revita a backbone procedural therapy with the potential to significantly reduce the burden of obesity, T2D and prediabetes. As we expand the adoption of Revita, we may seek regulatory allowance to evaluate additional indications and uses of Revita, as well as partnerships and/or distributor relationships for its commercialization in other global geographies.

Expand Application of Rejuva Platform to Other Metabolic Targets Beyond GLP-1

The Rejuva platform is modular and designed to enable local pancreatic production of key metabolic hormones important for proper beta cell function and incretin signaling. Our initial gene therapy candidates will include an AAV9 vector with a transgene that expresses GLP-1 (RJVA-001) and glucose-dependent insulinotropic polypeptide (“GIP”)/GLP-1 (RJVA-002) hormones from an insulin promoter. The modular nature of our platform can enable production of a number of additional metabolic hormones, including but not limited to, peptide YY (“PYY”) and amylin. The versatility of the Rejuva platform has the potential to underpin a comprehensive, next-generation modality capable of targeting the root causes of various metabolic diseases.

Addressing Interlinked Metabolic Conditions: Obesity and T2D

Metabolic syndrome represents a spectrum of disorders that are primarily characterized by disturbances in the body’s ability to properly metabolize glucose, lipids, and other essential molecules. One of the most prevalent and ubiquitous manifestations of metabolic syndrome is obesity, a condition where excessive body fat accumulates to a degree that has the potential to adversely impact health. The presence of excess body fat in obesity helps predispose at-risk individuals to other manifestations of metabolic disease, notably T2D, cardiovascular disease (“CVD”), metabolic dysfunction-associated steatohepatitis (“MASH”) (formerly known as non-alcoholic steatohepatitis).

Whereas our ancestors lived and adapted over centuries to ensure adequate energy supply in environments with limited nutrition, many 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. The mismatch between our ancestral genetics and modern diets that are high in fat and sugar is a primary driver of metabolic diseases in the recent past. Emerging scientific consensus links these high fat and sugar diets to dysfunction in key metabolic organs that increase the risk of the development of obesity and T2D, including the gut and pancreas. There is a high degree of overlap between obesity and T2D. Obesity is a key factor in poor metabolic function in patients with T2D, and weight loss is seen as a critical therapeutic goal for T2D patients. According to the American Diabetes Association Standards of Medical Care in Diabetes—2022, management of obesity is an important factor in the treatment of diabetes. According to the American Diabetes Association, even a 5% weight loss can improve blood glucose levels and reduce the need for medication. Therapeutic strategies that can both lower blood glucose and help with weight management could have longer-term benefits in prevention and remission of metabolic diseases.

Our Market Opportunity in Obesity

Obesity is a disorder of altered metabolic setpoint and nutritional excess characterized by progressive weight gain and metabolic dysfunction that sits at the apex of a diverse range of negative health conditions, including T2D, CVD, MASH, PCOS and certain types of cancer. The International Diabetes Federation estimates that there are over 800 million people globally today who suffer from obesity and prediabetes, with nearly 100 million people in the U.S. alone. With new innovations achieving greater degrees of potency than earlier agents, the obesity market is poised for immense growth, with industry expectations of approximately \$250 billion in drug sales by the end of the decade.

The human body has complex mechanisms to regulate weight, often compared to a thermostat that sets a “weight setpoint.” This setpoint is determined by a variety of factors, including genetics, environment and behavior, and is regulated by a multitude of neural and hormonal signals originating in the intestine, pancreas, and adipose tissue, converging in the hypothalamus and other regions of the brain.

In individuals with obesity, the weight setpoint might be set or defended at a higher level, which is a key challenge in the management of this disease. When an individual with obesity loses weight (either by behavior changes or with medications, including GLP-1 drugs), the body perceives the weight loss as a state of calorie deficit and risk of starvation. For this reason, the brain triggers a set of compensatory mechanisms, including increased hunger and decreased energy expenditure to try to restore the previous higher weight setpoint. The potential correction of the body’s altered metabolic setpoint can enable lasting benefits and translate to superior real-world outcomes.

The Current Treatment Paradigm in Obesity

Guidelines today focus on addressing excess weight in obesity, rather than developing strategies to lower or reset the body’s altered weight setpoint. Initial interventions focus on dietary changes and lifestyle modifications. The American College of Cardiology (“ACC”) and American Association of Clinical Endocrinologists (“AAACE”) recommend that patients with obesity should initially be prescribed aerobic exercise and resistance training, a reduced calorie diet, and

behavioral intervention. The AACE and ACC guidelines recommend that behavioral interventions be escalated for patients who do not achieve 2.5% weight loss within one month of beginning lifestyle modifications. If lifestyle modifications are not successful, treatment may move into therapeutic involvement and surgery. The AACE guidelines recommend that pharmacotherapy combined with lifestyle modifications be considered in individuals with a BMI of at least 27 kg/m².

The GLP-1 class of medicines have proven clinical efficacy in obesity. Wegovy (semaglutide), Saxenda (liraglutide), and Zepbound (tirzepatide) are GLP-1 based therapies currently FDA-approved for obesity, with additional candidates in various development stages. In August 2023, Novo Nordisk's SELECT trial demonstrated that treatment with semaglutide as an adjunct to the standard of care reduced the risk of heart attack, stroke, or heart disease-related death by 20% in overweight or obese individuals with CVD and no prior history of T2D. Current prescription trends suggest widespread usage of GLP-1s in obesity, demonstrating extensive patient interest in access to this class of drugs.

A critical unmet need remains in obesity despite the potency of GLP-1s. As with glucose control, GLP-1s have a “rebound effect” in obesity, in which weight loss is not maintained once medication is stopped. A 2022 third-party study exploring weight regain and cardiometabolic effects after withdrawal of 2.4 mg of once-weekly semaglutide found that participants regained two-thirds of their prior weight loss one year after treatment discontinuation, with similar changes in cardiometabolic variables. In July 2023, results from Eli Lilly's SURMOUNT trials for tirzepatide demonstrated similar results. We believe there remains a critical unmet need in obesity for a therapeutic option that provides long-term weight and metabolic benefit even after treatment discontinuation.

In an era of potent but non-durable weight loss therapies, we believe goals for anti-obesity medications should be 1) weight maintenance, defined as minimal weight regain over the course of at least one year after the discontinuation of therapy, and 2) obesity remission, defined as achieving durable weight loss without the need for ongoing obesity-specific pharmacologic or surgical treatments. Therapeutic strategies that can achieve weight maintenance and obesity remission have the potential to provide a step change in outcomes for patients with obesity.

Our Market Opportunity in Type 2 Diabetes

The International Diabetes Federation estimates that diabetes currently affects approximately over 500 million adults worldwide, with nearly 1.3 billion people expected to be living with T2D globally by 2050. In the U.S. alone, approximately 27 million people live with T2D on medical therapy and 5 million people live with advanced T2D on insulin therapy.

The Current Treatment Paradigm in T2D

The current standard of care for T2D is defined by life-long symptomatic management, focused on blood glucose control instead of disease modification. Even though T2D affects a significant fraction of the global population, there has not been a novel modality introduced to treat T2D in over a decade. While therapeutic advances in T1D have led to the approval of Tzield (teplizumab-mzwv) for the prevention of progression of T1D in 2022, and novel cell-based approaches to replacing beta cells in T1D, there has been an absence of therapeutic strategies tackling the root cause pathology of T2D. This lack of innovation is evidenced by the stubborn persistence of inadequate T2D control in patients. There are no approved disease-modifying therapies that target the organ-level root causes of T2D today.

The standard initial therapy in T2D is preventive 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 National Institute of Diabetes and Digestive and Kidney Diseases, 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. 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.

Several classes of oral and injectable drugs exist for the management of hyperglycemia, and the sequential addition of medications on top of one another is directed by patient preference and payor pressure to minimize costs. Most patients with T2D will remain on an expanding list of medications to lower their blood glucose throughout the remainder of their lives. The sodium-glucose cotransporter-2 inhibitor (“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 CVD 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 \$12 billion market and the GLP-1RA class an estimated \$20 billion market in 2022. 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. For example, GLP-1RAs impact several physiological processes and result in a variety of side effects, including nausea, vomiting and diarrhea.

The advent of the GLP-1RA class of medicines for T2D has led to an explosion in prescriptions of these drugs due to their impressive potency, cardiovascular benefits, and favorable weight loss profile. According to a report by Trilliant Health, physicians signed more than nine million GLP-1RA prescriptions in the U.S. for Ozempic, Mounjaro and Saxenda in the last three months of 2022 alone. However, a retrospective study conducted by Polonsky *et al.* analyzing medical claims data between July 2012 and January 2019 demonstrated that a majority of patients on a weekly GLP-1RA (i.e., semaglutide, dulaglutide or exenatide extended release) discontinued therapy at 12 months (Polonsky et al. *Diabetes Ther* (2022) 13:175–187). Discontinuation of these agents typically leads to an immediate loss of metabolic benefit and weight rebound, as seen in Eli Lilly’s SURMOUNT-4 study with tirzepatide and Novo Nordisk’s STEP-1 extension study with semaglutide. This lack of persistence to therapy and subsequent loss of benefit in both blood glucose and weight suggests that these agents do not offer durable disease modification and help explain the increasing burden of T2D in society, even with the availability of these potent drugs.

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 the same attention toward disease modification should be applied to T2D as is now already evident in T1D therapeutic development with goals of 1) diabetes prevention, defined as whether the treatment delays progression of diabetes, and 2) diabetes remission, defined as achieving a blood glucose level below the diabetic range for at least one year in the absence of active pharmacotherapy or ongoing procedures.

Our Approach

We design and develop novel, differentiated, disease-modifying therapies that precisely target and alter the function of the diseased organs responsible for obesity and T2D. Despite the development of highly potent medicines that can improve glucose control and weight loss, significant unmet needs remain in these diseases due to high rates of drug discontinuation over time, the loss of metabolic benefit upon drug discontinuation, and the inability of medicines to arrest the progressive nature of these conditions. Our vision is to develop transformative therapies that have the potential to prevent and eliminate metabolic diseases.

Our product candidates have the potential to offer a major advance in healthcare because they are designed as disease-modifying treatments that provide long-term metabolic benefits from a single administration, and are therefore potentially positioned to target the *prevention* and *remission* of disease. These critically important categories in obesity and T2D treatment cannot be addressed with current pharmacology. To be maximally impactful, these therapies must also be delivered at a scale that can match the incidence and prevalence of metabolic disease around the world. We believe our product candidates are not only unique in their potential for disease modification, but also in their design for broad accessibility for large populations. Accordingly, we believe our candidates have the capacity to revolutionize treatment of obesity and T2D and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

Our Solutions

We believe there is a significant market opportunity for disease-modifying treatments that provide long-term metabolic benefits across the spectrum of obesity and T2D and we are developing a suite of product candidates that will target different phases of these metabolic diseases.

Overview of Revita

Revita is an investigational outpatient procedural therapy designed to durably modify duodenal dysfunction, a major pathologic consequence of a high fat high sugar diet, which can initiate obesity and T2D in humans. The duodenum is the first segment of the small intestine and the first site of nutrient absorption within the body. The duodenal mucosa regulates the human metabolic response to food intake, and chronic exposure to modern diets high in fat and sugar drive a functional maladaptation of stem cells in the duodenum and lead to dysfunctional hyperplasia of the duodenal mucosa. These diet-induced changes to the structure and function of the duodenal mucosa disrupt physiologic nutrient sensing and signaling mechanisms from the gut to the brain, with resulting alterations to systemic metabolic activity that affect glucose control and satiety through multiple downstream organ systems. Emerging scientific consensus has identified this dysfunction in the gut as a root cause of obesity and metabolic dysfunction and therefore propose targeting gut dysfunction to address downstream metabolic diseases. There are no therapies approved today that target the duodenal mucosa for regeneration and renewal.

The Revita system is designed to enable durable and repeatable metabolic improvement by targeting duodenal dysfunction with an outpatient, endoscopic procedural therapy. Revita uses heat energy to ablate the dysfunctional duodenal mucosa, including the duodenal stem cells residing at the base of the mucosa, to enable regeneration and renewal of the duodenum and restore normal metabolic signaling from the gut. The Revita procedure provides thermal protection to the duodenum before ablating the superficial mucosa by (1) isolating the mucosa from the deeper muscle layer of the duodenum and then (2) hydrothermally ablating the superficial layer of the duodenal lining with a proprietary balloon catheter and control console. The procedure takes less than 45 minutes and can be conducted in an outpatient setting in a manner that allows immediate return to daily life for patients. 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 mechanisms.

Revita is designed to treat patients ranging from those who are living with obesity and at risk of developing metabolic complications of obesity, such as T2D, to those who have advanced T2D and have exhausted medical therapies. For individuals with obesity and prediabetes, Revita is designed to address upstream metabolic dysfunction that puts them at risk for the progression of obesity and at risk for the development of T2D.

Potential Benefits of Revita

We believe that Revita's unique individual features combine to provide a significantly differentiated solution to obesity, offering the following potential benefits:

- ***Durable and Repeatable Benefit.*** Revita is designed to improve metabolic health, blood glucose levels, and weight in patients living with obesity and/or T2D. A pooled analysis of data collected on secondary endpoints assessing weight in our previously conducted controlled clinical studies across the U.S. and Europe demonstrated a 3.4% (n=100) mean reduction in total body weight loss at four weeks in patients with T2D on multiple ADAs after undergoing a single Revita DMR procedure and showed a sustained mean body weight loss of 4.0% (n=94) at 48 weeks. We believe this is an important and differentiated therapeutic profile in obesity management. In addition, we believe our Revita system has the potential to enable repeat Revita procedures over time.
- ***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. Our proprietary Revita technology is designed to provide thermal protection before ablation, enabling isolation of the mucosa from deeper tissue structures and sparing pain fibers in the muscle while reducing risk of tissue injury.
- ***Broad Implementation.*** Revita is a modular system that can potentially be incorporated into the endoscopist workflow by leveraging familiar skillsets of advanced endoscopists. Revita is intended to fit into most

endoscopy suites and typically requires fewer than four cases for the endoscopist to acquire proficiency. It is designed to be an outpatient procedure that can be performed by a trained therapeutic endoscopist in less than an hour. Today, approximately over 25 million endoscopies are performed each year in the U.S., including over 600,000 advanced endoscopic procedures. Of the estimated 30 million people potentially on GLP-1s in the U.S. today, approximately 3 million will undergo an endoscopy this year. The Revita DMR procedure is designed to be a simple add-on procedure to these, and other endoscopies already performed on patients living with obesity and T2D annually.

- ***Real-World Outcomes.*** Because it is designed as a procedural therapy, Revita does not rely on perfect patient adherence or persistence to chronic therapy for its anticipated clinical effects. Unlike diet and lifestyle interventions or pharmacologic management, the benefits of Revita 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.
- ***Patient Friendly.*** Revita is designed to offer a straight-forward, outpatient experience requiring less than a half-day visit, and allowing patients to typically return to their normal daily lives the very next day. Furthermore, initial interim data suggest that the Revita DMR procedure has thus far been observed to be compatible with other current interventions for obesity in broad use, including diet and lifestyle, as well as existing and emerging pharmacologic therapies.

Overview of Rejuva

Rejuva is a novel, endoscopically administered, adeno-associated virus (“AAV”) pancreatic gene therapy platform designed to enable long-term remission of T2D and obesity by durably altering metabolic hormone production in the pancreatic islet cells of patients with T2D and obesity. Pancreatic islets are tiny clusters of cells distributed throughout the pancreas that play a crucial role in endocrine function and metabolism. There are several cell types within the pancreatic islet, including alpha cells responsible for glucagon production and beta cells responsible for insulin production. Metabolic dysfunction in obesity and prediabetes can lead to progressive beta cell dysfunction and eventual failure, loss of insulin production and secretion, and the development of metabolic disease. There are no therapies approved today that target the pancreatic islet in T2D or obesity.

The Rejuva platform is modular and consists of three key elements designed to enable successful pancreatic gene therapy delivery and expression with limited off-target biodistribution: (1) a novel, proprietary, investigational endoscopic device designed to enable local, low-dose therapeutic delivery directly to the pancreas (body and tail), (2) vectors with tropism for the pancreatic islet to enable successful transduction and (3) transgenes with tissue-restricted promoters driving the expression of metabolically active peptides that can durably impact glucose and weight control.

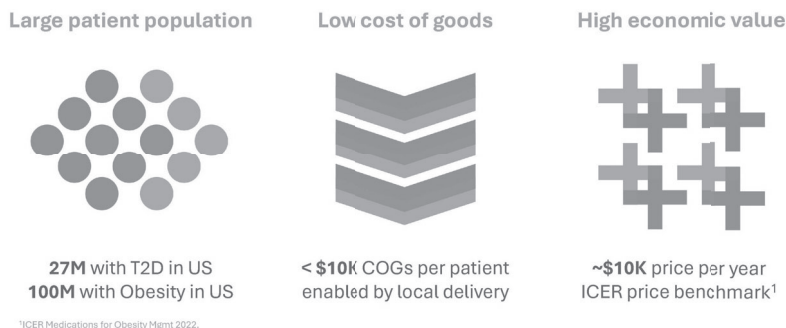
These peptides are intended to rejuvenate beta cell health, restore insulin production, and activate incretin signaling pathways in a nutrient-responsive (“smart”) manner. The first gene therapy candidate, RJVA-001, is comprised of an AAV9 viral vector that expresses a human GLP-1 hormone from an insulin promoter designed for the remission of T2D. The second candidate, RJVA-002, is designed to treat obesity and is composed of an AAV9 vector that expresses both human GIP and GLP-1 hormones driven by an insulin promoter. Activation of both GIP and GLP-1 receptors may improve body weight and blood sugar regulation.

Potential Benefits of Rejuva

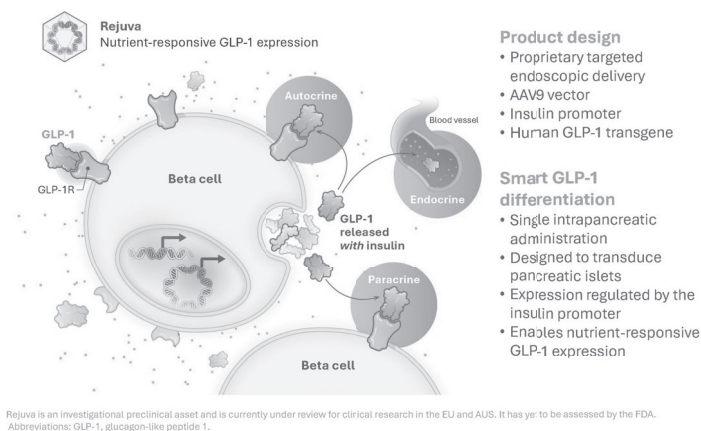
We believe that Rejuva’s individual features combine to provide a significantly differentiated solution to T2D and obesity, offering the following potential benefits:

- ***A Compelling, Substantial Commercial Model in Gene Therapy.*** We believe the Rejuva platform, if approved, has the potential to provide a differentiated market offering within the gene therapy space. We believe this potential for differentiation could be enabled by a large patient population (approximately 27 million people are living with T2D in the U.S.; approximately 100 million people are living with obesity in the U.S.), low cost of goods (local delivery of a validated AAV capsid enables a cost of goods sold of potentially less than \$10,000 per patient), and a development space where the high economic value is

substantial and well understood (approximately \$10,000 price per year under the Institute for Clinical and Economic Review price benchmark).



- Novel Approach to a Highly Validated Target.** Our Rejuva platform candidates leverage well established and understood hormone signaling known to be central to metabolic regulation. Our platform’s endoscopic pancreatic delivery, pancreas-targeted AAV capsid, and insulin promoter driven transgene expression enables nutrient-responsive (“smart”) production of GLP-1 (RJVA-001) and GIP/GLP-1 (RJVA-002) from beta-cells. Unlike GLP-1-based drugs, Rejuva candidates allow for durable physiologic metabolic hormone signaling.



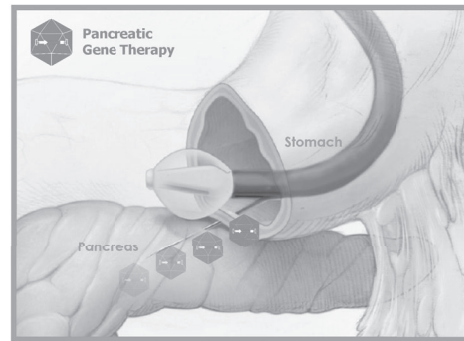
- Precise Local Delivery.** Our Rejuva gene therapy platform is designed to provide precise local delivery of gene therapy to the pancreas in a single endoscopic procedure. Our Rejuva platform leverages standard-of-care techniques for pancreatic tissue access and possesses key proprietary device elements and procedure steps, thereby reducing procedural risk. We believe our Rejuva gene therapy candidates will benefit from

localized administration, potentially avoiding the risk of high dose systemic administration that has been observed with other gene therapy candidates or GLP-1 receptor analogs.

Local delivery enables low viral genome dosing with limited systemic virus exposure¹

Islets are readily accessible^{2,3} via already established, routine, upper endoscopic ultrasound procedures,⁴ performed in ~300K patients per year in US⁵

Procedural risk is further mitigated with device design (e.g., needle size, volume, controlled infusion rate)



Endoscopic Procedure & PGTx Delivery

1. Rajagopalan et al. ASGCT 2022 oral presentation, Abstract no. 101. 2. Docherty & Russ. Encyclopedia of Tissue Engineering and Regenerative Medicine 2019, pp. 367-374. 3. Ravi et al. Medicine (Baltimore). 2021 Apr; 100(17):e25642. 4. Hasan & Hawes. Gastrointest Endosc Clin N Am. 2012 Apr;22(2):155-83. 5. Peary et al. Gastroenterology 2022 Feb; 152(2):621-644. PGTx~pancreatic gene therapy

- **Building Upon Clinical and Real-World Experience with Revita.** The gene therapy candidates from our Rejuva platform benefit from the extensive clinical and real-world experience that we have accumulated through our Revita program. Rejuva PGTx candidates can be delivered by the same treating physicians and in the same setting as the Revita DMR procedure, utilizing the same distribution network. Moreover, we believe the metabolic benefits of Rejuva PGTx candidates have the potential to be complementary to, and perhaps synergistic with, the Revita DMR procedure.
- **Rigorous Development Plan.** We completed key preclinical *in vivo* studies to support a CTA for RJVA-001 and subsequently submitted CTAs for RJVA-001 in T2D to regulators in the EU (Netherlands) and Australia in the second half of 2025, advancing the program toward its anticipated first-in-human study. We expect to receive regulatory feedback in the second quarter of 2026 and, subject to CTA authorization, to initiate first-in-human dosing of RJVA-001 and expected reporting of preliminary data in the second half of 2026.
- **Interchangeable Platform for Metabolic Therapy.** The Rejuva platform enables selection of multiple metabolically active peptide hormones (GLP-1, GIP, PYY, amylin, glucagon, etc.), either individually or in combination, with the same local delivery and plasmid construct for differential therapeutic profiles over time.

By employing Revita and Rejuva to target the prevention and remission of obesity and T2D, we believe it is possible to provide a step change in outcomes for patients above and beyond the current chronic management strategies that exist today. If we are able to obtain marketing authorization for these product candidates in the U.S., we believe these therapies will enable us to chart a course towards significantly reducing the burden of obesity and T2D globally.

Our Targets: the Gut and Pancreas

“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. An emerging consensus identifies the impact of modern diets on the gut as one of the body’s critical metabolic control systems as an important root cause of metabolic disease. The gut possesses the largest nervous system outside the brain, the largest hormone-producing endocrine system, a 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 a meal. These mechanisms work together to provide an early warning detection system that helps the body prepare for and respond to the food we ingest.

Diets have changed significantly over the past several decades, shifting from relatively calorie-poor, fiber-rich, natural foods to an inexpensive and abundant supply of ultra-processed foods high in simple fats and sugars. Our founders, along

with several scientific groups around the world, have detailed the specific changes that these modern diets cause in the gut and the downstream impact on the body and brain. While the gut has long been recognized as an acute nutrient sensor, its role in regulating the body's metabolic status over longer periods of time has been underappreciated. Recent advances have demonstrated that chronic exposure of the intestine to high levels of fats and sugars leads to structural and functional changes of the lining of the proximal gut that may signal a metabolic shift to the brain and body. These diet-induced changes are geographically confined to the upper small intestine, particularly the duodenum, an area directly accessible via routine upper endoscopy. This research provides, for the first time, an accessible potential target of pathology within the gut that sits at the apex of the complex metabolic changes underlying obesity and T2D.

Structural and functional changes in the duodenal lining

Studies analyzing the small intestine in diabetic patients and animal models have identified functional maladaptation of the intestinal mucosa after chronic dietary exposure to high concentrations of fat and sugar. Geltrude Mingrone (a consultant to the Company), 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 (West et al. bioRxiv preprint doi: <https://doi.org/10.1101/822122>). Aliluev and colleagues observed that high-fat, high-sugar diets alter intestinal stem cell homeostasis leading to hyperplasia of the duodenal mucosa (Aliluev et al. *Nat Metab.* 3(9):1202-1216). Studies in rodents chronically fed a high-fat diet have demonstrated up to a 50% increase in mucosal surface area compared with rodents fed a normal diet, illustrating diet-induced structural overgrowth over time. This finding of a nutrient-induced stem cell division process that causes structural and functional changes of the duodenal mucosa has been replicated by multiple independent groups in the U.S. and Europe, and across organism species and disease models. Michael Theodorakis et al. 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 (Theodorakis et al. *Am J Physiol Endocrinol Metab* 290: E550–E559, 2006).

Hyperplasia and dysfunction of the duodenum is associated with a greater surface area for nutrient absorption and altered neurohormonal signaling, changing the body's metabolic response from the gut. According to Duca et al., enteroendocrine cells in the duodenum respond to ingested nutrients by secreting hormones, including GLP-1 and cholecystokinin, which enter the circulation and trigger local nervous system activation. The brain receives these neurohormonal signals and uses the integrated information to regulate blood glucose levels and weight. In a healthy state, intraduodenal lipids trigger satiety and suppression of blood glucose, but chronic high-fat diets impair this gut-brain feedback, leading to metabolic dysfunction (Duca et al. *Cell Metab.* 2015 Sep 1;22(3):367-80, Duca et al., *Nat Commun.* 2021; 12: 903).

We believe that this preclinical and clinical evidence demonstrates that abnormal neurohormonal signaling from the duodenum is an important contributor to metabolic dysfunction, broadening conventional wisdom that excess weight and physical inactivity are the sole drivers of T2D.

Avoiding Nutrient Contact with the Duodenum can Reduce Insulin Resistance in T2D

The pancreas is a hormone-producing organ in the retroperitoneum surrounded by the duodenum, immediately below the stomach, with functions related to the secretion of digestive enzymes (exocrine pancreas) and hormones including insulin and glucagon from pancreatic islets (endocrine pancreas). Within the 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.

Most people can compensate for metabolic dysfunction by increasing insulin production to maintain normal blood glucose levels. Patients who develop T2D eventually experience a gradual loss of beta cell function, driven by two principal causes: (1) exhaustion of beta cell function in the face of longstanding metabolic dysfunction and chronically elevated blood glucose, and (2) damage to beta cells from the toxicity of circulating lipids (lipotoxicity). By the time the diagnosis of diabetes is made, patients have lost over 80% of their beta cell function, making early and aggressive intervention essential.

Increasing GLP-1 Levels in the Pancreas Can Improve Islet Metabolic Function

GLP-1 is a potent hormone produced in the distal intestine and secreted into the circulation in response to nutrient intake, and also produced in the pancreatic islets by alpha cells. The role of GLP-1 within the pancreatic islet in beta cell function and insulin production is one of the best understood hormonal mechanisms in medicine. The GLP-1 receptor is expressed in

beta cells, where activation acutely stimulates insulin secretion in response to blood glucose elevations and chronically stimulates insulin gene transcription and islet cell survival. The GLP-1 receptor is also expressed in alpha cells, where activation regulates glucagon expression. Studies have shown impaired GLP-1 signaling in the pancreatic islet in T2D, and that increased GLP-1 signaling can compensate for impaired insulin secretion, preserve beta cell function and survival, and improve glucose homeostasis. The beneficial effects of GLP-1 on islet function have been further demonstrated by the GLP-1RA class of medicines.

Revita and Rejuva are designed to treat obesity and T2D by directly targeting the gut and pancreas, respectively, addressing root causes of metabolic disease within these organs. By leveraging our expertise in developing novel, differentiated, disease-modifying 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 obesity and T2D.

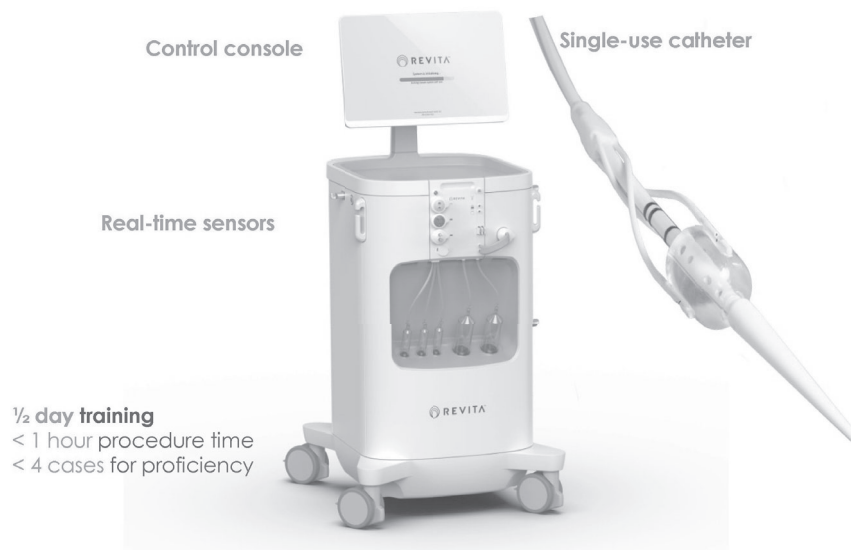
Revita Product Description

Revita Device Overview

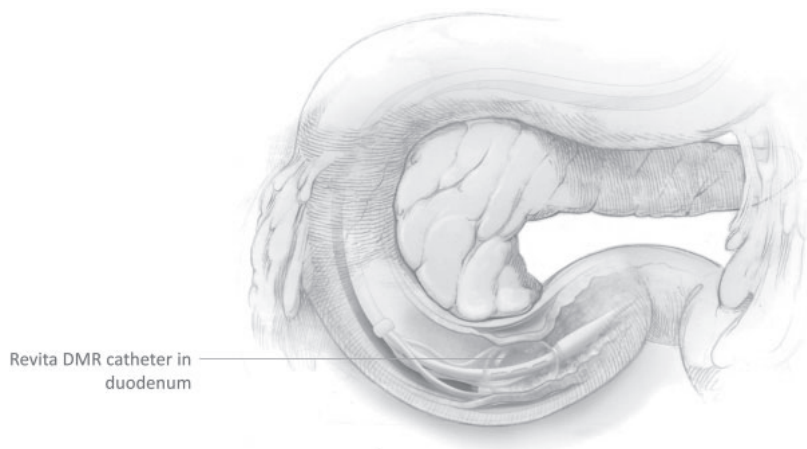
Revita comprises (i) the Revita console that houses our proprietary technology and software, and (ii) a single-use Revita DMR catheter. The console's touchscreen-based graphical user interface is designed to provide ease-of-use and clear guidance on the performance and progress of the procedure for the physician. The console is designed to control the flow, pressure and temperature of the ablative and cooling fluid, vacuum suction, facilitate the delivery of saline for the submucosal lift. 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 a proprietary safety mechanism that reduces 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 commercial console and catheter. The catheter and graphical user interface are currently being used in our REMAIN-1 and REVITALIZE-1 clinical studies, but the Revita console hardware below is not. We plan to seek FDA clearance of the proposed commercial system as part of our FDA De Novo process. The Revita DMR catheter comprises 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 only the mucosal and submucosal tissue into the port. The catheter is designed to be deliverable and trackable across the stomach into the small intestine over a standard endoscopic guidewire or the Revita procedurally optimized guidewire. In the first quarter of 2025, we began offering the FDA 510K cleared Revita

Guidewire to principal investigators to support ongoing Revita clinical studies. The Revita Guidewire is specifically designed for ease of delivery of the Revita DMR catheter.

Modular Revita Console



Revita is for investigational use only in the United States. Revita has a CE mark in the EU/UK. This is a rendering of a commercial prototype.



Revita Procedure Overview

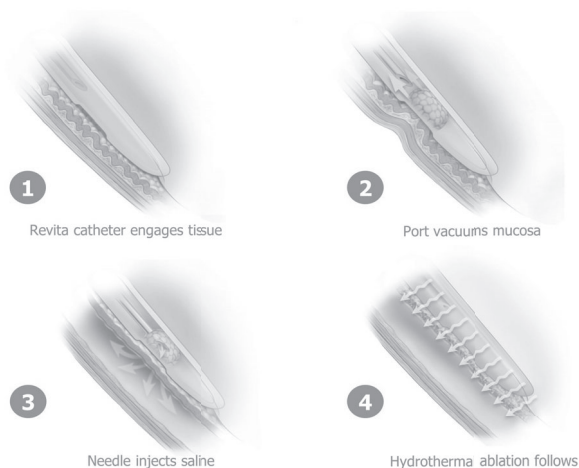
The Revita DMR procedure is designed to be a minimally invasive, outpatient, endoscopic procedural therapy using a proprietary balloon catheter that is uniquely designed for the duodenal mucosa in a procedure that typically lasts less than an hour. Revita is designed to target the mucosal surface for 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 thermal safety and hydrothermal ablation steps.

Thermal Safety. Our proprietary thermal safety procedural step involves an automated, circumferential injection 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. This procedure step is designed to create a thermal barrier between the mucosa and the underlying muscular layer in order to 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.

Designed to Create a Protective Thermal Barrier



Hydrothermal Ablation. After the thermal safety step 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 thermal safety 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 thermal safety 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 patient 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 over 500 participants across multiple clinical studies at sites in South America, Europe and the U.S. To date, we have observed the Revita DMR procedure, when added to certain ADAs and lifestyle counseling, to be generally well tolerated and demonstrated durable blood glucose lowering and weight stabilization in patients for two years post-procedure. We are currently evaluating the Revita DMR procedure in the REMAIN-1 weight maintenance program, which is designed to evaluate Revita’s potential to maintain weight loss following GLP-1 based therapy discontinuation.

Pursuant to our Strategic Reprioritization, announced on January 31, 2025, we paused investment in Revita for T2D, including the REVITALIZE-1 study and the Germany Real-World Registry study. Our decision to pause these studies was not driven by any safety or efficacy concerns. We continue to follow existing participants per protocol and report outcomes on an ongoing basis for these studies. For additional detail on REVITALIZE-1, see our Annual Report on Form 10-K for the fiscal year ended December 31, 2024. For additional detail on the Germany Real-World Registry study, see “Germany Real-World Registry Study” below.

The table below summarizes our ongoing, paused and completed clinical studies for the Revita DMR procedure.

Study and Status	Study Design	Primary Objectives	Upcoming Milestones
Ongoing			
REMAIN-1. Pivotal clinical study in participants who have lost at least 15% of their total body weight on GLP-1 therapy and wish to discontinue their GLP-1 without weight regain (ongoing)	<ul style="list-style-type: none"> Three Cohorts, multi-center, parallel cohort, randomized (2:1), open-label REVEAL-1/open-label: up to 40 participants Randomized midpoint analysis of 45 participants Randomized pivotal analysis: 315 participants (DMR and sham) 	<ul style="list-style-type: none"> To demonstrate superiority of the Revita DMR procedure to sham in weight maintenance after discontinuation of tirzepatide at 26 weeks To demonstrate that a majority of Revita DMR participants maintain clinically significant weight loss after discontinuing tirzepatide therapy at 26 weeks 	<ul style="list-style-type: none"> February 2026: Completed randomization in REMAIN-1 Pivotal Cohort Q2 2026: 1-year REVEAL-1 Cohort data Q3 2026: 1-year REMAIN-1 Midpoint Cohort randomized data Early Q4 2026: Topline 6-month randomized data from REMAIN-1 Pivotal Cohort Late Q4 2026: Potential FDA De Novo marketing application submission in post-GLP-1 weight maintenance.
Paused due to Strategic Reprioritization			
Germany Real-World Registry. Study in participants with inadequately controlled T2D on at least one ADA Commenced in April 2023 Announced on January 31, 2025 that Company paused investment	<ul style="list-style-type: none"> Prospective, post-market, clinical five-year follow-up of participants who have received the Revita DMR procedure in a real-world setting 	<ul style="list-style-type: none"> To assess the safety and clinical effectiveness, quality of life and participant reported outcomes, and healthcare utilization expenditure of the Revita DMR procedure 	<ul style="list-style-type: none"> Follow-up of participants who have received the Revita DMR procedure in a real-world setting and report data on an ongoing basis per protocol
REVITALIZE-1. Pivotal clinical study in participants with inadequately controlled T2D despite being on at least one GLA Commenced in March 2021 Announced on January 31, 2025 that Company has paused investment Converted to a safety only study, approved by FDA July 24, 2025	<ul style="list-style-type: none"> Stage 1: open-label, single-arm training stage Stage 2: Randomized, double-blind, crossover, sham-controlled, multi-center ~10-14 cm DMR Two arms: DMR and sham Stage 1: up to 140 participants Stage 2: up to 320 participants 	<ul style="list-style-type: none"> To demonstrate safety and tolerability of the Revita device and procedure 24 weeks post DMR 	<ul style="list-style-type: none"> Close study and report on safety H1 2027
Completed			
U.S. Pilot. Pilot study in participants with suboptimally controlled T2D despite being on metformin in combination with one to two additional OADs Completed (prematurely ended)	<ul style="list-style-type: none"> Randomized (2:1), double-blind, crossover, sham controlled, multi-center Two arms: DMR and sham 9 participants ~10 cm DMR No formal statistical powering 	<ul style="list-style-type: none"> Evaluate the safety and efficacy of the Revita DMR procedure on certain glycemic endpoints 	<ul style="list-style-type: none"> 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 participants with suboptimally controlled T2D despite being on an OAD and/or metformin Completed	<ul style="list-style-type: none"> Randomized, double-blind, crossover, sham controlled, multi-center ~10 cm DMR Two arms: DMR and sham 108 participants 	<ul style="list-style-type: none"> Evaluate the safety and efficacy of the Revita DMR procedure on certain T2D-related endpoints 	<ul style="list-style-type: none"> Baseline reduction of HbA1c, MRI-PDFF, HOMA-1R 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 participants on long-acting insulin Completed	<ul style="list-style-type: none"> Open-label, single-center ~15 cm DMR Single arm 16 participants 	<ul style="list-style-type: none"> Evaluate the feasibility of eliminating insulin therapy in T2D participants by combining the Revita DMR procedure with a GLP-1 and lifestyle counseling 	<ul style="list-style-type: none"> 69%, 56% and 53% of participants 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 participants with poorly controlled T2D despite at least one OAD Completed	<ul style="list-style-type: none"> Open-label, multi-center ~9 cm DMR Single arm 46 participants 	<ul style="list-style-type: none"> Evaluate the safety and effectiveness of the Revita DMR procedure on certain glycemic endpoints 	<ul style="list-style-type: none"> Baseline mean HbA1c reduction of 0.9% at 24 weeks ($p^* < 0.001$) Baseline mean reduction in total body weight of 3.1% sustained through two years ($p = 0.01$) The Revita DMR procedure was generally well tolerated
Revita. First-in-Human. Clinical study in participants with poorly controlled T2D despite at least one OAD Completed	<ul style="list-style-type: none"> Open-label, single-center Single arm: LSDMR (~9 cm) and SSDMR (~3 cm) 57 participants 	<ul style="list-style-type: none"> Evaluate the safety and feasibility of the Revita DMR procedure over variable lengths of the duodenum 	<ul style="list-style-type: none"> 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 participants 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:

- **Total Body Weight Change.** A physical measurement from baseline weight identifying alteration in weight due to caloric excess or deficit. Total body weight change can include weight gain (from energy excess) or weight loss (from energy expenditure exceeding caloric intake).
- **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 (“OGTT”), evaluates beta cell function after a participant 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, OGTT is the calculation of the total excess of blood glucose measured during the course of the OGTT.

Revita Clinical Program Insights

Our Revita clinical program design has been informed by our prior clinical studies and expertise in the field of metabolic diseases, including obesity and T2D. We are evaluating and/or have evaluated the Revita DMR procedure in over 500 participants, 30 clinical centers, with the procedure performed by more than 30 different endoscopists. We have followed most Revita-1 and Revita-2 participants beyond 12 months post-procedure to observe the long-term safety of the Revita DMR procedure, including its effects on glucose homeostasis and weight. Based on these experiences, we believe the Revita DMR procedure has the potential to:

- enable weight maintenance in patients living with obesity;
- reduce the risk of developing diabetes in patients with high-risk prediabetes;
- improve glycemic control in T2D patients on insulin; and
- improve glycemic control in T2D patients on one or more ADAs who are not yet on insulin.

We are focused on developing Revita to treat patients ranging from those who are living with obesity and at risk of developing metabolic complications of obesity, such as T2D, to those who have advanced T2D and have exhausted medical therapies. For individuals living with obesity and prediabetes, Revita is designed to address upstream metabolic dysfunction that puts them at risk for the progression of obesity and at risk for the development of T2D.

Ongoing REMAIN-1 Clinical Study

We are evaluating Revita in the REMAIN-1 weight maintenance program, which is designed to evaluate Revita’s potential to maintain weight loss following GLP-1 based therapy discontinuation. The REMAIN-1 program includes three distinct participant cohorts that are conducted under a single IDE:

The REVEAL-1 Cohort (n=22): an open-label study in individuals with obesity who have lost at least 15% of their total body weight on a GLP-1 medication and who either need or choose to discontinue GLP-1 therapy. After stopping the GLP-1 based therapy, participants receive Revita treatment in an open-label setting and take part in a structured diet and lifestyle program. REVEAL-1 is designed to provide early, real-world insights on how Revita performs after GLP-1 discontinuation.

The REMAIN-1 Midpoint Cohort (n=45): a randomized, double-blind, sham-controlled pilot study to assess the potential of Revita to maintain weight loss after GLP-1 based therapy discontinuation. Participants with obesity who have not yet taken GLP-1 drugs, are initiated on tirzepatide at the time of enrollment, and treated with the drug to achieve at least 15% total body weight loss. Participants then discontinue tirzepatide and are randomized to undergo either Revita or a sham procedure with a 2:1 treatment randomization. The key efficacy endpoint is total body weight change in Revita versus sham

at 3 months. The randomized Midpoint Cohort serves as an important early randomized readout to assess Revita’s potential to maintain weight loss after GLP-1 based therapy discontinuation. All participants enrolled in the study will receive diet and lifestyle counseling.

The REMAIN-1 Pivotal Cohort (n=315): a randomized, double-blind, sham-controlled pivotal study to evaluate the safety and efficacy of Revita in maintaining weight loss after GLP-1 based therapy discontinuation. Participants with obesity who have not yet taken GLP-1 drugs, are initiated on tirzepatide at the time of enrollment, and treated with the drug to achieve at least 15% total body weight loss. Participants then discontinue tirzepatide and are randomized to undergo either Revita or a sham procedure with a 2:1 treatment randomization. The first co-primary endpoint is defined as the percent of total body weight regain from the time of tirzepatide discontinuation in Revita versus sham participants through 6-month follow up. The primary objective is to demonstrate a benefit of Revita versus sham for weight maintenance after GLP-1 based therapy discontinuation. The second co-primary endpoint evaluates a responder rate among the Revita treated participants at 1 year to demonstrate the durability of the Revita procedure for weight maintenance after discontinuation of a GLP-1 based therapy. The responder rate is defined as the percentage of participants who received the Revita procedure who maintain at least 5% total body weight loss from pre-tirzepatide (week -21) to week 52. Secondary objectives will include evaluation of the effectiveness of the Revita DMR procedure on the change in blood glucose levels, CVD risk factors, body composition and pre-diabetes status. All participants enrolled in the study will receive diet and lifestyle counseling.

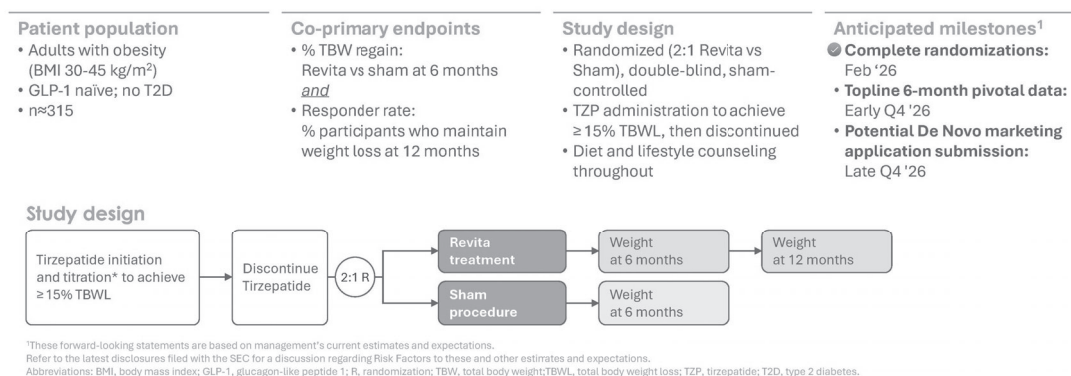
Enrollment of all three cohorts is complete. We completed randomization of 307 participants in the REMAIN-1 Pivotal Cohort in February 2026, with topline six-month data anticipated in the early fourth quarter of 2026. In March 2026 we received pre-submission feedback from the FDA in which it acknowledged that the safety profile of the Revita DMR System, based on clinical data from over 300 procedures, is consistent with a Class II device classification. We anticipate submitting a potential De Novo marketing application in post-GLP-1 weight maintenance in the late fourth quarter of 2026.

In September 2024, the FDA approved an amendment to the clinical study protocol for the REMAIN-1 study of our Revita device, which aligns the co-primary endpoint with a weight maintenance indication for Revita and adds a midpoint analysis at three months allowing us to analyze and report on approximately 45 randomized participants. In the third quarter of 2024, we initiated REMAIN-1.

In July 2024, we obtained Breakthrough Device designation from the FDA for the Revita system, as an adjunct to diet and exercise, to perform hydrothermal ablation of the duodenal mucosa, or the Revita DMR procedure, for use in the maintenance of weight loss after discontinuation of GLP-1-based therapy on participants who cannot tolerate long-term GLP-1 therapy and who are not candidates for endoscopic remodeling procedure or bariatric surgery.

We gained FDA approval for the IDE in the first quarter of 2024 to initiate the pivotal REMAIN-1 study.

The table below depicts the REMAIN-1 pivotal clinical study design.



REVEAL-1 Cohort:

In December 2025, we announced 22 participants had been treated in the REVEAL-1 cohort, with up to six months of follow-up data available for 17 participants. As of December 2, 2025, no safety or tolerability concerns were reported, consistent with Revita’s safety profile observed in prior clinical experience. Participants maintained stable weight after a single Revita procedure, with a mean total body weight change of 1.5% ± 1.3% (SEM; n=17) at 6 months. Published third-

party studies report ~10% weight regain by this time point after GLP-1 withdrawal alone. Minimal change in HbA1c levels was observed after the Revita procedure ($0.04\% \pm 0.08\%$; SEM; $n=17$), compared to the ~0.4% increase in HbA1c seen post-GLP-1 based therapy discontinuation in the STEP-1 trial extension of GLP-1 withdrawal. These results indicate the potential for Revita to help stabilize cardiometabolic parameters beyond weight loss alone. Mean body weight and HbA1c curves showed a stable and durable trajectory over time, consistent with prior Revita clinical study and real-world experience. No procedure-related serious adverse events were observed; 8 of 22 participants (36%) experienced mild treatment-emergent adverse events which were transient, and self-limited; all consistent with prior Revita experience and similar to routine upper endoscopy findings.

In June 2025, we announced positive 3-month data from the REVEAL-1 Cohort. As of June 23, 2025, 22 participants had been treated in the REVEAL-1 Cohort, with 3-month follow-up data available for 13 individuals. The profile of the REVEAL-1 Cohort closely mirrors that of the REMAIN-1 Midpoint and Pivotal Cohorts, with an average age of 49 and a gender distribution of 11 women and 2 men. All participants had previously been treated with a GLP-1 therapy for durations ranging from approximately 5 months to 3 years, with a median total body weight (“TBW”) loss of 20.9% while on therapy. Fifteen percent of participants had pre-diabetes at baseline. At 3 months, 12 of 13 participants either lost or maintained their weight after GLP-1 based therapy discontinuation and a single Revita procedure. Notably, 6 of 13 experienced further weight loss. Median weight remained stable through 3 months (TBW change of 0.46% / ~ 1 pound was within the margin of error for daily weight measurement), compared to the typical 5-6% (10–15 pounds) rebound seen in other third party clinical studies such as SURMOUNT-4. Only one participant experienced weight regain similar to that seen after tirzepatide withdrawal. Early signs also point to excellent weight stability following Revita procedure, with essentially no weight change between 1 and 3 months (median weight gain at 1 month: 0.43% and 3 months: 0.46%). Consistent with prior studies of Revita, the procedure was well tolerated, with no unanticipated or serious adverse effects reported. No new safety concerns were observed.

In April 2025, we announced additional positive early data from the REVEAL-1 Cohort. As of April 1, 2025, 15 participants had been treated with Revita, with 1-month follow-up data available for the first 7 participants. There were not any safety or tolerability concerns reported in the 15 participants treated to date, consistent with Revita’s favorable safety profile from pooled data across more than 100 treated participants. At 1-month post-procedure, 7 participants experienced an average weight regain of just 1.2%, compared to the ~3% typically observed at this time period after GLP-1 based therapy discontinuation based on prior clinical studies.

In January 2025, we reported positive preliminary results from the REVEAL-1 open-label cohort. Initial findings from the first participant, as of a cutoff date of January 13, 2025, showed successful weight maintenance at one month following GLP-1 based therapy discontinuation and Revita DMR procedure.

REMAIN-1 Midpoint Cohort:

In January 2026, we announced 6-month randomized data. As of January 29, 2026, across the prespecified efficacy population ($n=40$, with five participants excluded per protocol due to diet and lifestyle noncompliance and only included in the safety population), Revita-treated participants experienced a 4.5% weight regain vs 7.5% in the sham arm at 6 months ($p=0.07$, one-sided), consistent with meaningful and sustained attenuation of the expected post-GLP-1 rebound trajectory. An exploratory analysis of participants who achieved above median weight loss during GLP-1 run-in ($n=20$) showed that Revita-treated participants experienced 4.2% weight regain versus 13.3% with sham at 6 months, corresponding to an approximately 70% relative reduction in post-GLP-1 weight regain (LS mean difference -9.1% ; $p=0.004$, one-sided). As expected, treatment-by-run-in weight loss interaction terms suggested a meaningful relationship between degree of GLP-1-associated weight loss and the magnitude of Revita benefit. Further post-hoc analysis in March 2026 demonstrated a statistically significant correlation between ablation length and weight maintenance in the Revita arm and that more complete duodenal ablation drives greater treatment effect ($n=29$; $p=0.048$). Putting both together, in participants with above median GLP-1-induced weight loss who received greater than 14 cm duodenal ablation, Revita participants retained 88% of GLP-1 induced weight loss at six months compared to only 60% in sham participants. Revita continued to demonstrate favorable safety and tolerability results through six months, with no treatment-emergent serious adverse events related to the device or procedure, and no study discontinuations due to adverse events. No new related adverse events were observed between 3- and 6-month follow up.

In September 2025, we announced positive 3 -month results from the randomized REMAIN-1 Midpoint Cohort ($n=45$), demonstrating Revita’s potential to maintain weight loss after discontinuation of GLP-1 based therapy. Enrollment for this cohort had been previously completed, and as of September 26, 2025, all participants had been treated. The study met its 3-month efficacy endpoint with strong statistical significance ($p=0.014$), delivering 2.5% further weight loss with Revita ($n=29$) even after stopping tirzepatide, versus 10% weight regain in sham-treated participants ($n=16$). These results are

clinically and statistically significant and provide randomized, blinded evidence that drug-free, durable weight maintenance is possible. No Revita-related SAEs or Grade II+ AEs were observed. Side effects were infrequent, mild, and transient, consistent with prior Revita clinical study experience.

In the fourth quarter of 2024, we completed enrollment of the 45 participants of the randomized REMAIN-1 Midpoint Cohort.

REMAIN-1 Pivotal Cohort:

We completed enrollment of the REMAIN-1 Pivotal Cohort in July 2025. We completed randomization of the REMAIN-1 Pivotal Cohort in February 2026, with topline six-month data anticipated in the early fourth quarter of 2026. In March 2026 we received favorable FDA feedback on our De Novo classification request for Revita and anticipate submitting a potential De Novo marketing application in Post-GLP-1 weight maintenance in the late fourth quarter of 2026.

Germany Real-World Registry Study

In April 2023, we initiated the Germany Real-World Registry study, a prospective, post-market, clinical follow-up study to evaluate the Revita DMR procedure in participants with inadequately controlled T2D. Our inclusion criteria included participants ages 18 and over, with a baseline HbA1c between 7.0% and 10.0%, a BMI of less than or equal to 45 and on at least one ADA. The study assessed change in HbA1c, change in number of ADAs, safety and tolerability, quality of life and participant reported outcomes, and healthcare utilization expenditure over five years in participants with T2D after receiving the Revita DMR procedure in a real-world setting.

On January 31, 2025, we announced that pursuant to the Strategic Reprioritization, we have paused investment in the Germany Real-World Registry study. We expect to continue to follow the existing participants per protocol and continue to report on clinical, health economic, and participant-relevant outcomes from this study on an ongoing basis.

As of October 31, 2025, the first 30 participants with 1 year of follow-up had, at baseline, a mean age of 60 years, a mean weight of 102 kg (225 lbs; BMI 33 kg/m²), and a mean HbA1c of 8.8%, despite being on up to three glucose-lowering agents (“GLAs”).

After a single Revita procedure, these 30 participants achieved a mean total body weight loss of 8.0% with weight decreasing from 102 kg to 94 kg at 3 months, a result that was sustained throughout 1 year post-procedure (94 kg) (Table 1, Figure 3). Notably, 28 of 30 participants lost weight, 20 of 30 participants experienced at least a 5% weight reduction, and 12 of 30 participants saw weight reductions of 10% or more. In parallel, mean HbA1c decreased by 1.0% at 3 months, from 8.8% at baseline to 7.7%, and this improvement was sustained throughout 1 year post-procedure (7.9%) (Table 1) with 83% (25/30) of participants on stable or reduced GLAs. In this cohort, weight loss and glucose improvements began as early as one month after the Revita procedure and were sustained through 1 year of follow-up (Table 1).

Table 1. Germany Real-World Registry Study Weight and Blood Sugar Data Post-Revita Procedure (n=30)

Endpoint	Baseline	3 Months	6 Months	1 Year
Weight (kg)	102 ± 3.4	94 ± 3.3	94 ± 3.3	94 ± 3.3
HbA1c (%)	8.8 ± 0.2	7.7 ± 0.4	7.9 ± 0.3	7.9 ± 0.2

Mean ± standard error of the mean (“SEM”) values shown. Fractyl Health internal data.

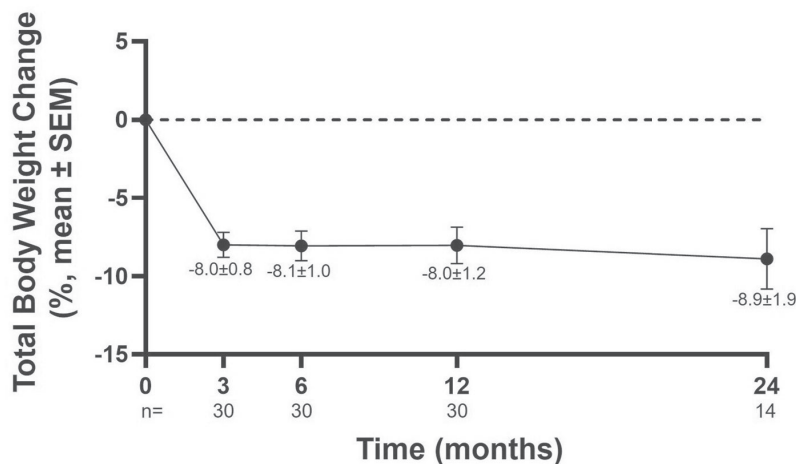
Of these 30 participants, 14 have now been followed for 2 years post-procedure. These 14 participants had a mean age of 62 years, mean weight of 104 kg (229 lbs; BMI 34 kg/m²), and a mean HbA1c of 9.1%, despite being on up to three GLAs. These 14 participants achieved a mean weight loss of 7.9% at 1 year with weight decreasing from 104 kg to 95 kg, an improvement that was maintained through 2 years post-procedure (94 kg) (Table 2). Mean HbA1c reduced by 1.2% at 1 year, from 9.1% at baseline to 7.8%, and this improvement was sustained throughout 2 years post procedure (7.4%) (Table 2), with 86% (12/14) of participants on stable or reduced GLAs.

Table 2. Germany Real-World Registry Study Weight and Blood Sugar Data Post-Revita Procedure (n=14)

Endpoint	Baseline	3 Months	6 Months	1 Year	2 Years
Weight (kg)	104 ± 5.7	96 ± 5.5	96 ± 5.3	95 ± 5.3	94 ± 5.3
HbA1c (%)	9.1 ± 0.4	8.1 ± 0.7	8.2 ± 0.5	7.8 ± 0.3	7.4 ± 0.3

Mean ± SEM values shown. Fractyl Health internal data.

Figure 1: Germany Real-World Registry Study Total Body Weight Change from Baseline



Medication use was recorded at baseline and each follow-up visit. Changes were categorized as initiation or discontinuation of any GLA or anti-obesity medication class. In this Germany Real-World Registry study, treatment adjustments reflected routine clinical management and were not protocol-mandated. At baseline, participants were on up to 3 GLAs prior to treatment with Revita with inadequately controlled T2D. 40% of participants were already receiving a glucagon-like peptide-1 receptor agonist (“GLP-1RA”) for glucose control and remained inadequately controlled despite treatment. During follow-up, 14 of 30 (47%) participants remained on stable GLAs through their last follow-up period, 11 of 30 (37%) participants decreased the number of GLAs from baseline, and only 5 of 30 (17%) participants increased the number of GLAs from baseline. Analyses of weight and HbA1c were stratified by the change in the number of GLAs from baseline to account for the potential confounding effects of concomitant pharmacotherapy.

When stratifying for medication adjustments post-baseline, participants who were on either stable or reduced medications (n=25) had similar effects on weight and HbA1c at 1 year and 2 years post-procedure compared to the entire cohort. Those participants on stable or reduced medications had a mean weight reduction of 8.4±1.3% and 8.8±2.2% compared to 8.0±1.2% and 8.9±1.9% for the entire cohort (Figure 1 above) at 1 year and 2 years post-procedure, respectively. Likewise, participants on stable or reduced medications had a mean HbA1c reduction of 0.9±0.3% and 1.7±0.4% compared to 0.8±0.3% and 1.7±0.4% for the entire cohort at 1 year and 2 years post-procedure, respectively. Thus, the sustained improvement in weight and HbA1c observed after Revita occurred despite a substantial reduction in average GLA use and cannot be attributed to new medication use during the Germany Real-World Registry study follow up period.

Participant-reported outcomes (“PROs”) revealed that Revita was valued by participants and improved T2D management. At 1 year and 2 years post-procedure, 97% and 93% of participants, respectively, reported that they would undergo the Revita procedure again, and 100% and 93% of participants, respectively, would recommend the procedure to a family member or friend (n=30 at 1 year; n=14 at 2 years post-procedure). Revita received a mean score of 9.8±0.1 and 10±0.0 (1-10 scale, 10 highest) for its ability to improve T2D management. Revita’s ability to improve quality of life was scored a mean of 9.6±0.2 and 10±0.0 by Germany Real-World Registry study participants at 1 and 2 years post-procedure, respectively.

No device- or procedure-related serious adverse events have been reported to date.

Collectively, these findings highlight the potential of a single Revita treatment to deliver durable weight maintenance, glucose improvement, and reduction in medication utilization without significant adverse events in a real-world setting out to 2 years post-procedure. Parallel PROs demonstrate durable participant-perceived value and improvement in T2D management.

As of February 15, 2025, we had treated 39 participants with Revita DMR and enrolled 34 participants in the Real-World Registry study with 12-month follow-up data from 17 participants. At baseline, prior to Revita DMR procedure, these participants (n=17) were a mean age of 61 years, with obesity and advanced T2D, a mean body weight of 106 kilograms (234 pounds; BMI 34 kg/m²) and mean baseline fasting blood glucose (FBG) and HbA1c of 181 mg/dL and 9.1%, respectively, despite using up to three GLAs. Approximately 65% of these participants were male. At three months, participant mean weight was reduced by 7.2 kilograms (16 pounds) and this reduction was maintained through 6 and 12 months post-procedure (see the table below for absolute values). Nearly all participants lost weight with 65% and 29% losing >5% and >10% of their body weight at 12 months post-Revita DMR procedure, respectively. Weight loss was observed as early as one-month post-Revita DMR procedure, and weight loss was generally maintained through one year of follow-up, further underscoring in a real-world setting the potential for a single Revita DMR procedure to be a compelling and durable weight maintenance solution.

FBG and HbA1c also improved, with mean decreases of 50, 47, and 49 (n=17) mg/dL and 1.0, 1.0, and 1.2% (n=17), at 3, 6, and 12 months, respectively. In addition, at 12 months post-procedure, 82% of participants stabilized or reduced their GLA usage in addition to losing weight and improving their hyperglycemia (n=17). PROs revealed that Revita was valued by participants and improved T2D management. At 12 months post-procedure, 94% of participants reported they would undergo the Revita DMR procedure again and 100% would recommend the procedure to a family member or friend (n=17). Revita scored a 9.7 and 9.3 (1-10, 10 highest) for its ability to improve T2D management and quality of life, respectively (n=17). As of February 15, 2025, no device or procedure-related serious adverse events have been reported.

The table below reflects the Germany Real-World Registry study Weight and Blood Sugar Data Over Time Post-Revita DMR procedure.

Endpoint	Baseline	3 Months	6 Months	12 Months
Weight (kg)	106	99	99	99
FBG (mg/dL)	181	130	133	132
HbA1c (%)	9.1	8.1	8.0	7.9

Mean values shown. Company data on file, n=17. NCT06256497. HbA1c=glycated hemoglobin.

REVITALIZE-1 Pivotal Clinical Study

We obtained Breakthrough Device designation from the FDA for the Revita DMR System to perform the Revita DMR procedure to improve glycemic control and reduce insulin needs in T2D patients who are inadequately controlled on long-acting insulin. In granting Breakthrough Device designation, the FDA found the following: there is a reasonable expectation that Revita will provide for more effective treatment of 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.

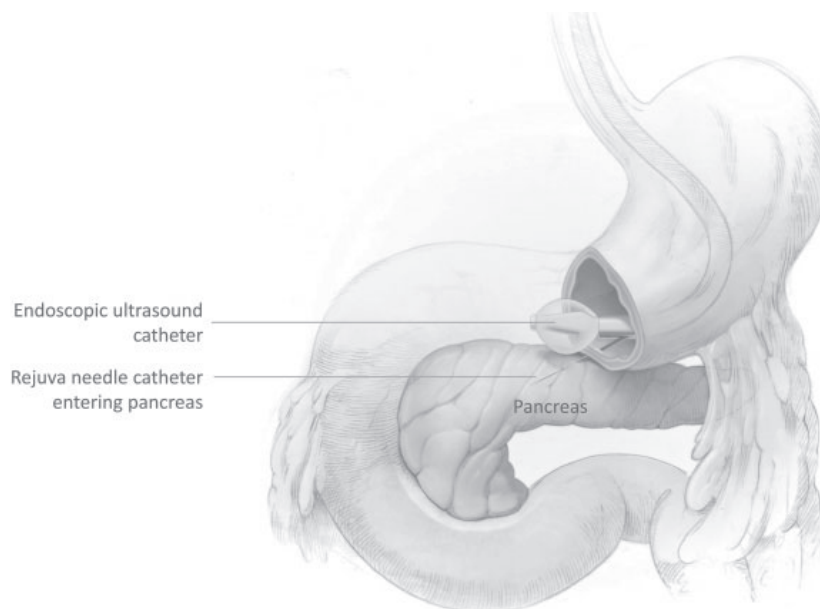
On January 31, 2025, we announced that pursuant to the Strategic Reprioritization, we paused investment in REVITALIZE-1, and our decision to do so was not driven by any safety or efficacy concerns for Revita in T2D. At that time, enrollment was paused and on July 24, 2025 FDA agreed to and approved the final study revision converting the study to safety only and reducing the overall size to those participants already enrolled, establishing participant follow-up to 24 weeks post Revita procedure. Participants previously enrolled and randomized were those with inadequately controlled T2D, and who were on at least one GLA. Participants randomized to the sham arm were offered an opportunity to receive the Revita DMR procedure (crossover) once unblinded. Participants who elected to crossover and undergo the Revita DMR procedure are being followed per protocol.

In June 2024, the FDA approved an amendment to the protocol of the REVITALIZE-1 study of our Revita device, which expanded eligibility to participants with T2D who are inadequately controlled on any GLA, including GLP-1 drugs and/or insulin.

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 participants with inadequately controlled T2D despite being on up to three ADAs and 20 to 100 units of insulin daily.

Rejuva Platform Description

Rejuva is a modular, physiologic gene therapy platform with three key elements designed to enable successful pancreatic gene therapy: (1) a proprietary delivery catheter designed to enable local, low dose therapeutic delivery directly to the pancreas via endoscopic access, (2) vectors with tropism for the pancreatic islet to enable successful transduction and gene delivery with limited biodistribution via this route of administration, and (3) transgenes with tissue-restricted promoters and metabolically active peptides that can durably impact glucose and weight control. Rejuva is designed to directly administer a gene therapy into the pancreas with both mechanical and molecular confinement of the therapeutic candidate with local administration and tissue-specific promoters.



Rejuva Device Overview

The Rejuva catheter leverages a single-use Rejuva PGTx catheter with a pressure-regulated and flow rate-controlled automated delivery mechanism. We believe the catheter enables a targeted delivery process by enabling a proprietary safety mechanism that controls the parameters of delivery that are required to ensure minimal disruption to the pancreatic tissue, and potentially reduces the risk of physician error by automating certain steps of the treatment process by guiding the fluid delivery mechanism. The Rejuva catheter is further composed of a narrow 27-gauge needle catheter that can be delivered through the working channel of a standard endoscopic ultrasound in which needle size, bevel shape, and aperture are designed to minimize risk of injury to the pancreas upon needle insertion.

Rejuva Drug Overview

The Rejuva drug platform is designed to be a modular, interchangeable platform composed of delivery vectors with high tissue tropism for the pancreatic islet and tissue-restricted promoters confining metabolically active transgene expression to islet cells. In the first quarter of 2024, we nominated RJVA-001, our first clinical candidate to emerge from the Rejuva platform for the remission of T2D. RJVA-001 combines a novel, proprietary Rejuva catheter for delivery, an AAV9 serotype vector, and a proprietary transgene construct, which features a modified human insulin promoter and a proprietary coding sequence that enables secretion of active human GLP-1.

In the fourth quarter of 2024, we nominated our first smart GIP/GLP-1 pancreatic gene therapy lead candidate, RJVA-002, designed for the treatment of obesity. RJVA-002 is a locally administered AAV9 viral vector that expresses human GLP-1 and GIP hormones from a human insulin promoter. RJVA-002 is designed to activate both GIP and GLP-1 receptors, which play crucial roles in regulating blood sugar and body weight.

Our GLP-1 PGTx candidates are designed to express GLP-1 specifically in beta cells in a manner that will allow beta cells to produce, package, and secrete GLP-1 hormone in a similar method to insulin. In this way, the GLP-1 transgene product can act within the pancreatic islet on adjacent alpha and beta cells to augment local GLP-1 receptor activation and signaling. Because of this local expression, our GLP-1 PGTx candidates are designed to improve beta-cell health and function and thereby provide durable weight loss and glycemic control while minimizing the side effects of systemic exposure to GLP-1.

Smart GLP-1 gene therapy, targeted to pancreatic islets, may offer differentiated benefit

β -cell machinery can be leveraged to produce nutrient-stimulated hormones^{1,2}

Islet cells are terminally differentiated,³ making adeno-associated virus (AAV) suitable for durable effect

Opportunity to amplify islet GLP-1 signaling to improve β -cell health

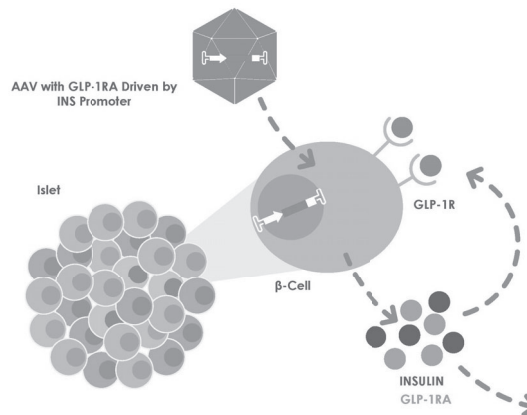


Figure adapted from Saikia et al. JCI Insight. 2021 6:e1418511. 1. Lubczewski et al. Keystone 2023 oral presentation, Poster no. 1025. 2. Rajagopalan et al. ADA 2023 oral presentation, Abstract no. 181-OR. 3. Perit et al. J Clin Endocrinol Metab. 2010 95: E234-E239. GLP-1=glucagon-like peptide 1, GLP-1R=GLP-1 receptor, GLP-1RA=GLP-1R agonist, INS=insulin.

Rejuva Delivery Overview

Our Rejuva PGTx candidates are locally administered using a proprietary needle catheter that is uniquely designed for pancreas delivery in an outpatient, endoscopic procedure that lasts approximately twenty minutes. The procedure is performed by a trained endoscopist while the patient is under conscious sedation or general anesthesia. With the help of the Rejuva catheter handle, 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 Rejuva catheter through the working channel of an endoscopic ultrasound imaging device and into the stomach. Ultrasound will be used to direct needle placement through the stomach wall into the body and tail of the pancreas after identifying the pancreatic duct and other key anatomical structures. The needle is then advanced into the distal pancreas. The physician will confirm needle placement before enabling a precise dose of the drug candidate to be delivered into the pancreas by an automated syringe pump system in the console. During the administration, the catheter handle will control the pressure and flow rate of the delivered fluid to prevent injury to the tissue and regulate the volume of delivery to control the precise dose of administration. A favorable benefit-risk profile of the delivery device can be enabled by directing the needle toward the body and tail of the pancreas, where a majority of pancreatic islets reside, and by avoiding the pancreatic duct in the head of the pancreas.

Preclinical Data Overview: Rejuva Gene Therapy Platform

We have evaluated potential GLP-1 PGTx candidates in large and small animal studies. In survival studies in over 100 large animals, we have observed 100% technical success with our Rejuva device using our proposed clinical route of administration with no device-related adverse events observed thus far. In small animal pharmacology studies, we observed that our potential GLP-1 PGTx candidates were generally well tolerated, reduced weight, improved glycemic control, and delayed T2D progression compared to vehicle or control and semaglutide. Given the data observed in our preclinical studies thus far, we believe that our Rejuva gene therapy candidates have the potential to provide superior clinical benefit in T2D and people living with obesity who currently have limited treatment options that provide long-term benefit even after treatment discontinuation.

Preclinical Studies: Proof-of-Concept

RJVA-001:

The lead product candidate from this platform, RJVA-001, is being advanced for patients with inadequately controlled T2D. RJVA-001 is designed to durably reprogram pancreatic beta cells to locally produce GLP-1 under nutrient-responsive

control, potentially enabling physiologic hormone secretion without the high circulating levels that contribute to side effects seen with systemic GLP-1 drugs.

In the second half of 2025, we completed preclinical chemistry, manufacturing, and controls activities and lot release for our RJVA-001 drug product, as well as key preclinical *in vivo* studies to support a CTA. During the same period, we submitted CTAs for RJVA-001 in T2D to regulators in the EU (Netherlands) and Australia, advancing the program toward its anticipated first-in-human study. We expect to receive regulatory feedback in the second quarter of 2026 and, subject to CTA authorization, to initiate first-in-human dosing of RJVA-001 and expected reporting of preliminary data in the second half of 2026.

In June 2025, we presented new preclinical data from Rejuva at the American Diabetes Association’s (“ADA”) 85th Scientific Sessions. We demonstrated that a single dose of GLP-1 PGTx was well-tolerated in healthy normal weight mice and prevented weight gain and hyperglycemia following a switch to a high-fat diet. Importantly, these data highlight Rejuva’s distinct mechanism of action. The Smart GLP-1™ design of Rejuva enables nutrient-responsive secretion, exerting minimal physiologic effect under healthy metabolic conditions and only activating in the presence of metabolic stress. This targeted activity, which mimics the body’s endogenous GLP-1 physiology, highlights the potential for Rejuva to offer superior potency and tolerability.

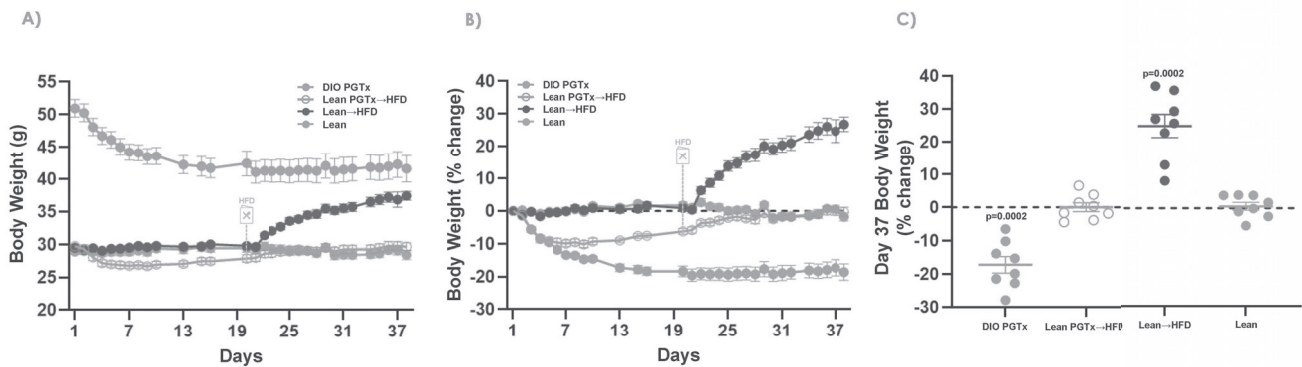
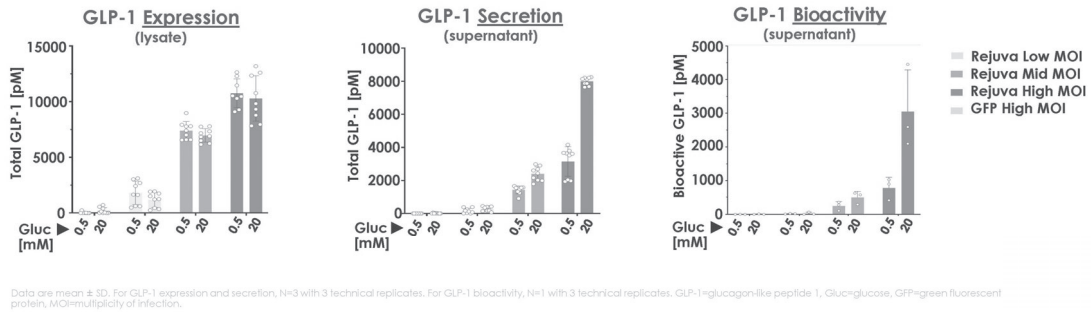


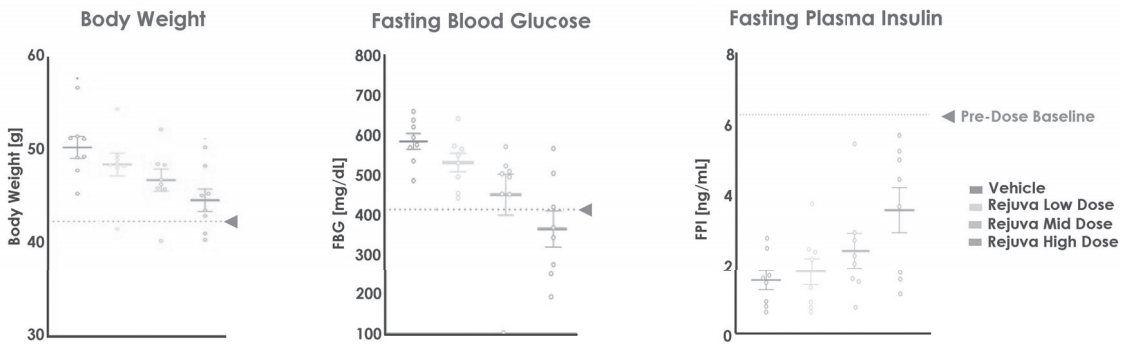
Figure 3. Single-Dose GLP-1 PGTx reduced Body Weight in Diet-Induced Obesity Mice and Prevented Weight Gain in Lean Mice Challenged with High-Fat Diet. GLP-1 PGTx was well-tolerated in diet-induced obesity (DIO) and lean mice. In the DIO PGTx cohort, GLP-1 PGTx reduced body weight (BW) by 20% at day 21 (B) and maintained weight loss through day 37 on high-fat diet (HFD) (-17%) (A, B and C; p=0.0002). BW at day 37 increased by 25% in the Lean→HFD cohort when switched to HFD (A, B and C; p=0.0002). However, in the Lean PGTx→HFD group, BW was reduced by 6% at day 21 (B), and did not rise above baseline after the HFD switch (A, B and C). Data are reported as mean absolute and percent change from baseline ± standard error of the mean, n=8 per group. HFD=high-fat diet.

In May 2025, we presented new preclinical data from Rejuva in an oral session at the American Society of Gene and Cell Therapy 2025 Annual Meeting. These data showed that a single-dose RJVA-001 led to durable, dose-dependent metabolic improvements in a well-established mouse model of diabetes (db/db). Additionally, these data highlight the platform's potential to deliver durable, nutrient-responsive GLP-1 secretion from pancreatic beta cells, mimicking natural hormone regulation with low circulating levels of GLP-1, offering a potentially profound mechanistic advantage over pharmacologic GLP-1 drugs.

Rejuva Shows Nutrient Responsive, Dose-Responsive GLP-1 Expression and Secretion in Transduced Human Beta Cells

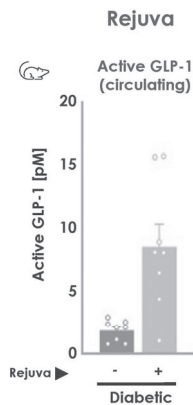


Rejuva GLP-1 Improves Metabolic Control in db/db Mice Dose-responsive improvement in body weight, blood glucose, and insulin levels



- Rejuva administered in db/db mice at 8 weeks of age (advanced T2D model)
- All data from day 46 post-single IP AAV injection (durable, dose-responsive PD effects)

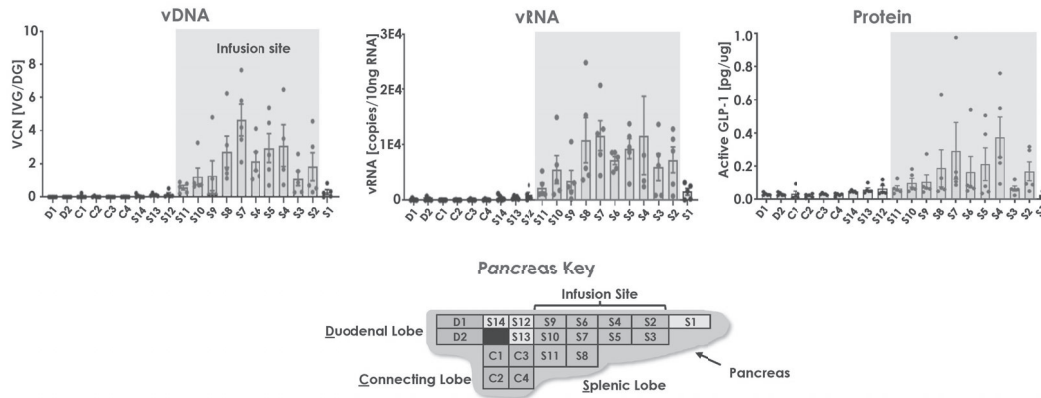
Data are mean \pm SEM, n=6 per group. FBG=fasting blood glucose, FPI=fasting plasma insulin, GLP-1=glucagon-like peptide 1, T2D=type 2 diabetes, IP=intraperitoneal, PD=pharmacodynamic, AAV=adeno-associated virus.



Data are mean \pm SEM, n=6 per mice group from day 44 post IP AAV injection. Levels detected at highest Rejuva dose tested in db/db mice. Circulating GLP-1 levels in db/db mice were more than twice those of healthy controls (db/+) (data on file).

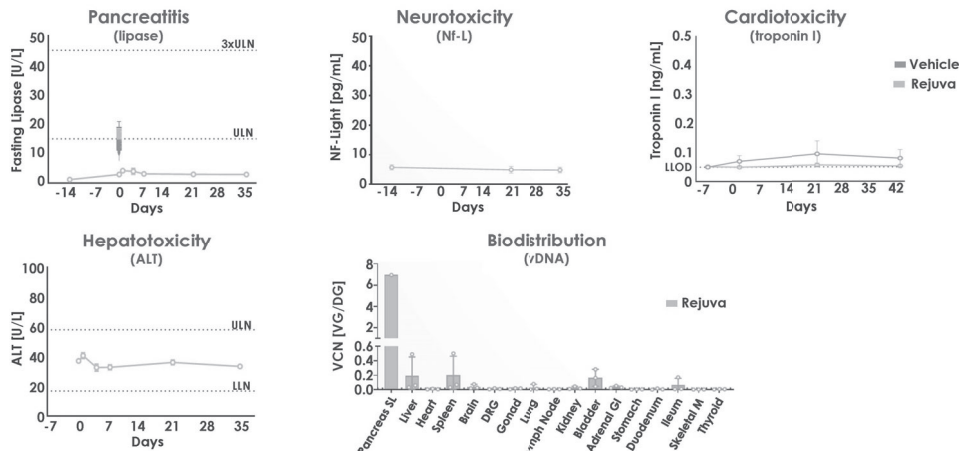
In a porcine route-of-administration safety model, RJVA-001 also showed strong efficacy, targeted delivery, and a favorable safety profile with no serum, biodistribution, or histopathologic findings of concern reinforcing its readiness for first-in-human studies.

Rejuva AAV Effectively Delivered to Pancreas Via Targeted ROA Transgene DNA, RNA, active GLP-1 protein enriched in targeted pancreatic splenic lobe



Data are mean \pm SEM, n=5 pigs. VCN, RNA, and GLP-1 protein averaged across pancreatic biopsy sections. VCN=vector copy number, GLP-1=glucagon-like peptide 1, VG/DG=vector genome/diploid genome, ROA=route of administration.

No Toxicity Observed Following Rejuva Treatment No serum, biodistribution, or histopathologic findings of concern

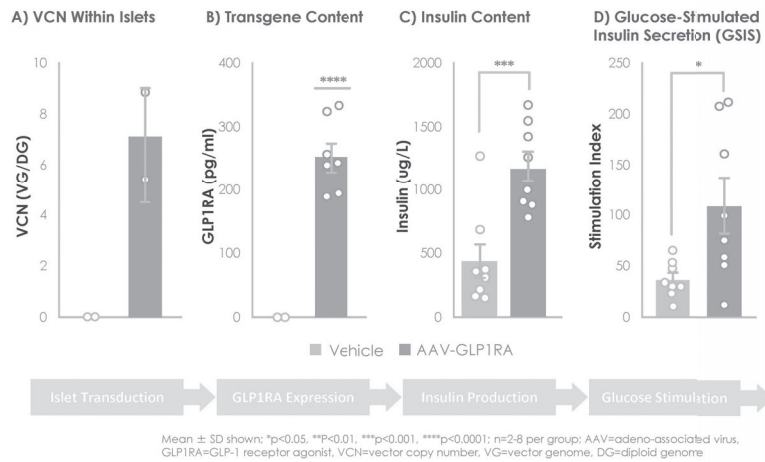


Data are mean \pm SEM, n=2-4 pigs per group. ALT=alanine transaminase, NF-L=neurofilament light chain, ULN=upper limit of normal, LLN=lower limit of normal, VCN=vector copy number, VG/DG=vector genome/diploid genome.

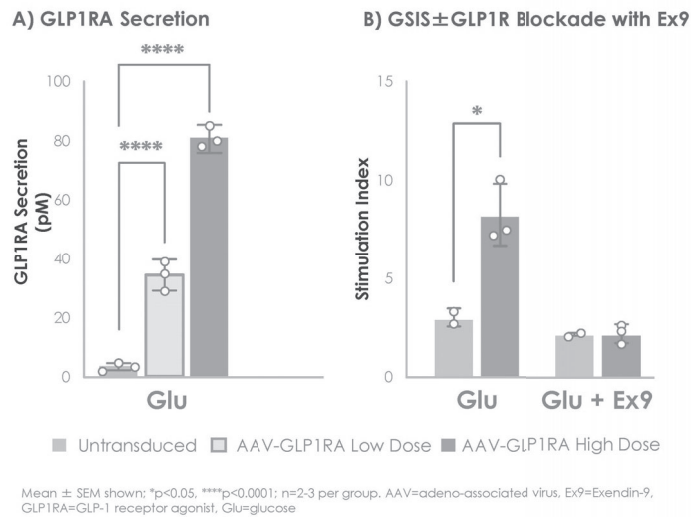
In the first quarter of 2025, we achieved alignment with European authorities on a patient population and study design for the RJVA-001 first-in-human study. The upcoming Phase 1/2 first in human study is designed to be an open-label, multicenter, single ascending dose study evaluating the safety, tolerability, and preliminary efficacy of RJVA-001 in adults with inadequately controlled T2D despite use of multiple glucose-lowering agents, including GLP-1 receptor agonists. Participants will undergo a standardized medication run-in and GLP-1 washout before receiving RJVA-001 delivered via endoscopic ultrasound-guided intrapancreatic infusion utilizing our investigational delivery device. The preliminary study design comprises three escalating dose cohorts (up to 3 participants each) which will be followed by an optional expansion cohort of up to 20 additional participants treated at the selected optimal dose. Participants will be monitored for 12 months for safety, glucose control, immune response, and GLP-1 expression, and enrolled in a long-term follow-up study for up to five years. Primary endpoints include safety and tolerability. Secondary endpoints include change in HbA1c, fasting plasma

glucose, and time-in-range as measured by continuous glucose monitoring. Exploratory endpoints assess beta-cell function, metabolic biomarkers, cardiovascular risk markers, and transgene expression.

We have conducted multiple proof-of-concept studies with GLP-1 PGTx candidates consisting of AAV-delivered transgenes carrying an insulin promoter driving GLP-1RA sequences in *in vitro*, *ex vivo* human islets, *ex vivo* mouse islets, and *in vivo* survival studies in a *db/db* mouse model of T2D and obesity. In *db/db* mice 10 weeks after a single administration of a GLP-1 PGTx candidate, we observed dose-dependent expression of the GLP-1RA protein in whole pancreas explants and in isolated islets from animals sacrificed at that time point. Isolated pancreatic islets from treated mice grown *ex vivo* demonstrated increased insulin content and improved glucose-stimulated insulin secretion (“GSIS”), a hallmark of improved beta cell function.



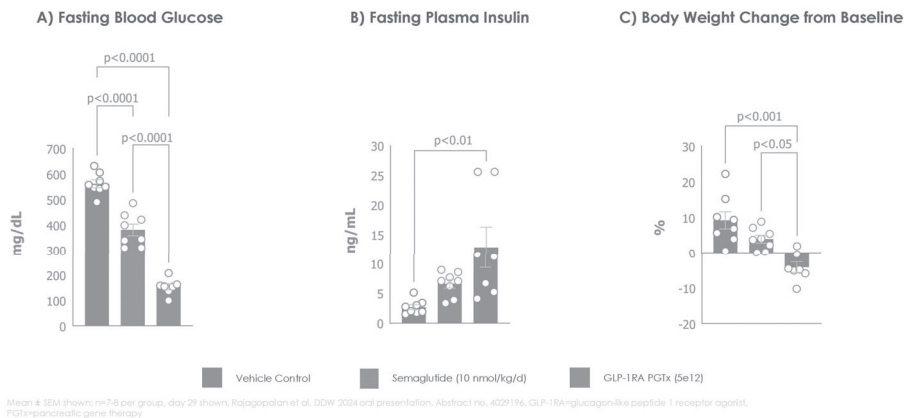
In the human EndoC-BH5 beta cell line, a GLP-1 PGTx candidate demonstrated dose-dependent increases in GLP-1RA secretion into the cell supernatant and improved GSIS. The improvement in GSIS was blocked by the administration of a GLP-1 receptor antagonist (exendin-9), demonstrating that improvements to beta cell function by the GLP-1 PGTx candidate were achieved through GLP-1 receptor binding and activation, and demonstrating the potential for pharmacologic agents that block the GLP-1 receptor to abrogate the effects of RJVA-001.



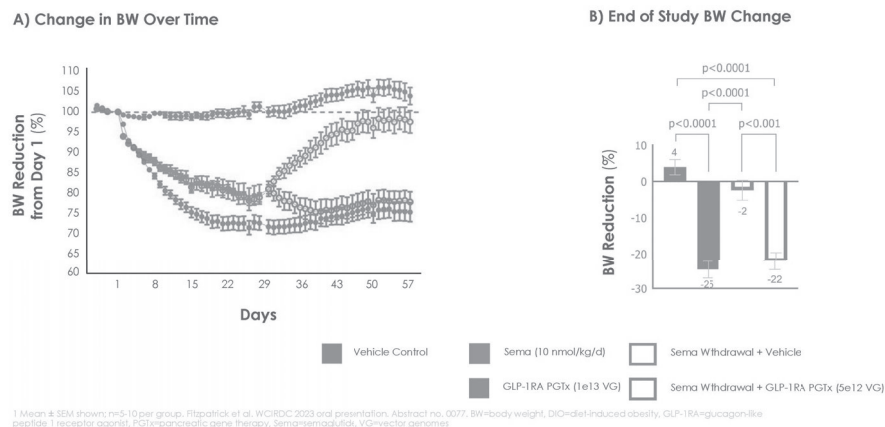
In *ex vivo* human islets, a GLP-1 PGTx candidate demonstrated dose-dependent transduction of up to 25% of beta cells within islets along with a doubling of GSIS. Taken together, we believe the results from EndoC-BH5 and healthy (non-diseased) human islets indicate that GLP-1 PGTx candidates have the potential to successfully transduce human beta cells and improve beta cell function even in healthy, non-diseased islets.

In proof-of concept preclinical *in vivo* studies in a *db/db* mouse model, we evaluated escalating doses of GLP-1 PGTx candidates in glucose lowering potency compared to vehicle. We observed dose-dependent improvements in FPG that were sustained for 64 days after a single administration of a GLP-1 PGTx candidate compared to vehicle control, along with sustained increases in fasting insulin at the same time point. We believe these results indicate that GLP-1 PGTx candidates have the potential to improve glucose control and beta cell insulin production and secretion in a durable manner.

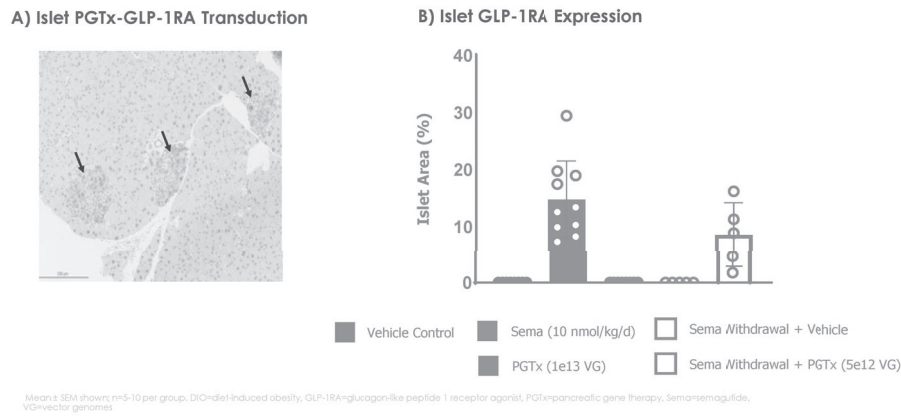
In a head-to-head preclinical *in vivo* study in a *db/db* mouse model, we evaluated a GLP-1 PGTx candidate compared to semaglutide. By four weeks post treatment, we observed a statistically significant average reduction of FPG of 73% ($p < 0.0001$), a statistically significant increase in fasting insulin of 478% ($p < 0.01$), and a statistically significant decrease in total body weight of 14% ($p < 0.001$) relative to vehicle treated mice after a single administration of a GLP-1 PGTx candidate. Based on these data, we believe this study suggests that a single administration of a GLP-1 PGTx candidate can achieve greater improvements in blood glucose control and weight loss and delayed T2D progression in *db/db* mice compared to semaglutide.



In a head-to-head preclinical *in vivo* study in a DIO mouse model, we evaluated weight loss after a single administration of GLP-1 PGTx candidate compared to semaglutide 10 nmol/kg daily. At 28 days after administration, we observed a statistically significant reduction of total body weight of 27% for the GLP-1 PGTx candidate compared to 21% for semaglutide ($p < 0.05$ for the difference between GLP-1 PGTx candidate and semaglutide). Semaglutide-treated animals were then randomized on day 29 to withdrawal of semaglutide or a single administration of the GLP-1 PGTx candidate, and both groups were followed for an additional 4 weeks. On day 57, we observed weight loss of 25% in the obese rodents initially treated with the GLP-1 PGTx candidate, compared to weight gain of 4% in vehicles. Animals withdrawn from semaglutide regained weight to a net 2% body weight loss on day 57, while animals who crossed over from semaglutide to a single dose of the GLP-1 PGTx candidate maintained body weight loss on day 57 with 22% weight loss from baseline. Based on this data, we believe that a single administration of a GLP-1 PGTx candidate can achieve greater improvements in weight loss than semaglutide at the tested dose, durable improvements in weight loss compared to vehicle control, and can offer a potential weight maintenance therapeutic solution to prevent weight regain after semaglutide discontinuation.

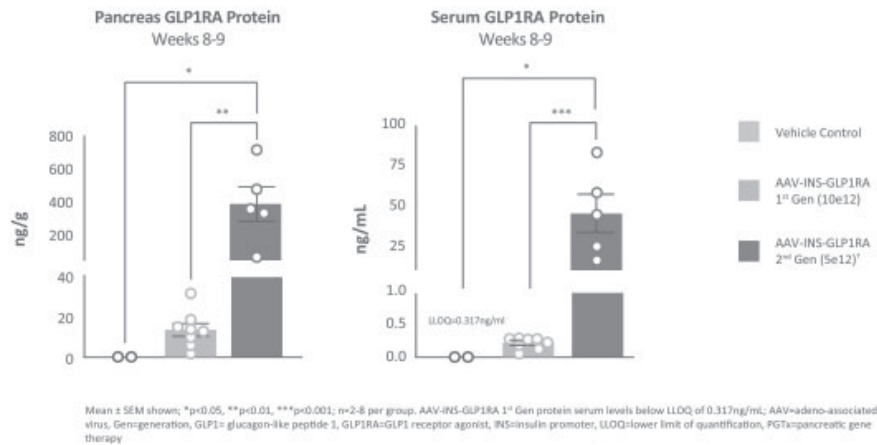


In vivo studies of GLP-1 PGTx candidates in DIO and *db/db* mice have demonstrated high specificity of transgene expression for the pancreatic islets with no detectable transgene expression in off-target tissues (e.g., the exocrine pancreas). Quantification of GLP-1RA immunoreactivity in mouse islet beta cells indicates that potent efficacy can be achieved with only a small fraction (< 10%) of beta cells expressing GLP-1RA.

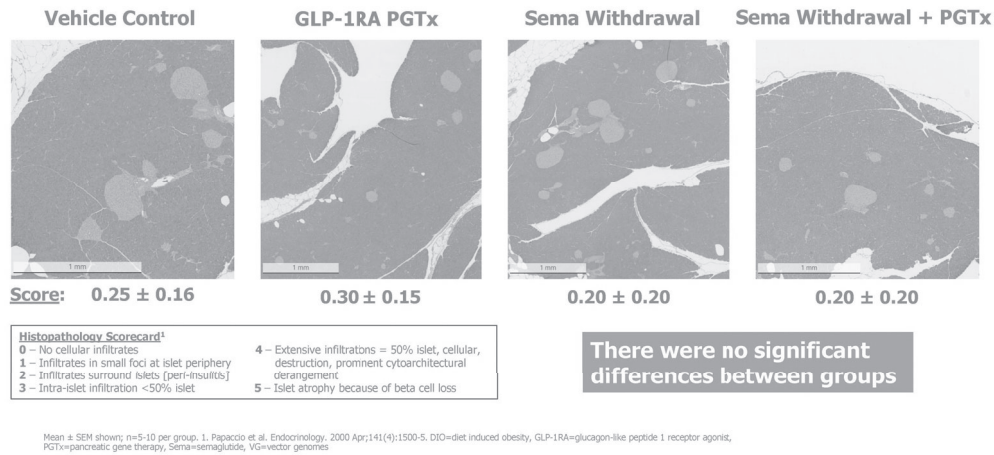


We observed that promoter and regulatory element optimization in GLP-1 PGTx candidates demonstrated the potential for a broad dynamic range of transgene protein production at eight to nine weeks after a single administration of a GLP-1 PGTx candidate. We believe these results indicate that GLP-1 PGTx candidates have the potential to provide durable metabolic benefits after a single administration with limited systemic exposure.

GLP-1 PGTx Candidate Pancreas Protein Expression and Serum Levels
 Promoter and regulatory element optimization demonstrated potential for broad dynamic range of transgene protein production



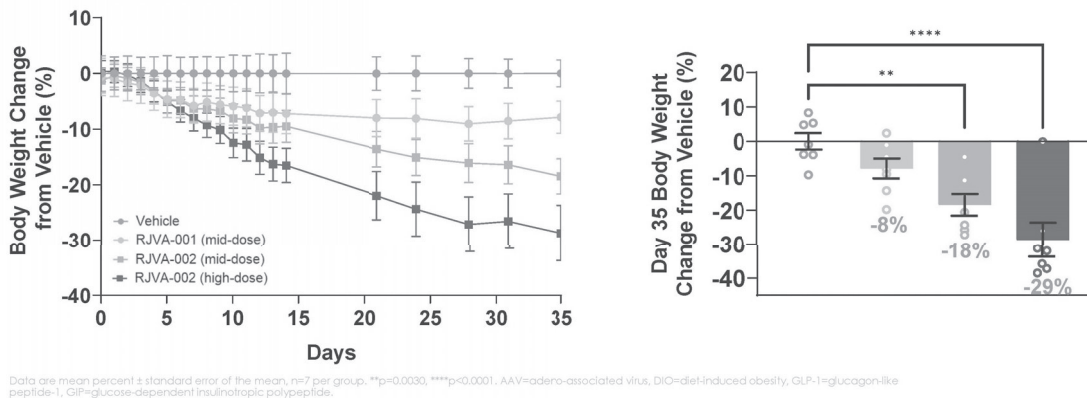
No abnormal findings were observed in animal behavior or clinical chemistries. Histopathologic analysis showed no evidence of inflammation, pancreatitis or pancreatic cancer.



RJVA-002:

The Company’s second candidate from the Rejuva platform, RJVA-002, is a dual GIP/GLP-1 gene therapy and is currently in preclinical development. RJVA-002 expands the Rejuva platform into obesity, targeting dual incretin biology with the goal of achieving durable, well-tolerated, weight loss from a single intervention.

In October 2025, we announced new preclinical potency data from RJVA-002 at the 2025 Cell & Gene Meeting on the Mesa. These data expand the potential of the Rejuva platform from the durable treatment of T2D to obesity. In this ongoing preclinical study, male mice engineered to express a humanized GIP receptor (“Biocytogen”) were fed a 60% high-fat diet (“HFD”) to induce obesity and were then randomized into one of four treatment cohorts: vehicle control, RJVA-001 mid-dose, RJVA-002 mid-dose, and RJVA-002 high-dose (n=7 per group). A single administration of RJVA002 led to approximately 30% weight loss over five weeks in a translational obesity model in male mice, with weight loss not yet plateaued and no observed adverse effects. In this preclinical trial, all mice were continued on HFD for the duration of the study. Treatment with RJVA-002 resulted in a robust, dose dependent reduction in body weight compared to vehicle control. By day 35, mice in mid- and high-dose cohorts had lost a mean of 18% (p<0.01) and 29% (p<0.0001) of their body weight after a single dose of RJVA-002, respectively. These findings highlighted the potential for a durable, one-time gene therapy approach to obesity that could match or exceed best-in-class chronic drug therapy. Results from this ongoing study at longer time points and with associated metabolic measurements will be presented at an upcoming scientific congress.



Clinical Development Overview: Rejuva Gene Therapy Platform

We completed key preclinical *in vivo* studies to support a CTA for RJVA-001 and subsequently submitted CTAs for RJVA-001 in T2D to regulators in the EU (Netherlands) and Australia in the second half of 2025, advancing the program toward its anticipated first-in-human study. We expect to receive regulatory feedback in the second quarter of 2026 and, subject to

CTA authorization, to initiate first-in-human dosing of RJVA-001 and expected reporting of preliminary data in the second half of 2026.

In addition, in the fourth quarter of 2024, we nominated our first smart GIP/GLP-1 pancreatic gene therapy lead candidate, RJVA-002, designed for the treatment of obesity. RJVA-002 is a locally administered AAV9 viral vector that expresses human GLP-1 and GIP hormones from a human insulin promoter. RJVA-002 is designed to activate both GIP and GLP-1 receptors, which play crucial roles in regulating blood sugar and body weight.

Commercialization Strategy

The Revita DMR System is approved in Europe as a medical device under a CE Mark and has received reimbursement authorization through NUB in Germany for the treatment of T2D. After securing reimbursement for Revita in 2022, in the first half of 2023 we initiated a limited commercial pilot in a single center in Dusseldorf, Germany, along with a Germany Real-World Registry study, designed to evaluate real-world evidence of Revita's safety and effectiveness in people with inadequately controlled T2D. We have paused investment in this commercial pilot, as well as in ongoing enrollment in the Germany Real-World Registry study.

In the U.S., we have obtained Breakthrough Device designation from the FDA for the Revita DMR System, as an adjunct to diet and exercise, to perform hydrothermal ablation of the duodenal mucosa, or the Revita DMR procedure, for use in the maintenance of weight loss after discontinuation of GLP-1-based therapy on patients who cannot tolerate long-term GLP-1 therapy and who are not candidates for endoscopic remodeling procedure or bariatric surgery. 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 market authorizations but does not alter or confer any advantage in the regulatory review, approval, or clearance standard for medical devices.

We intend to submit a De Novo classification request with FDA for Revita after we complete the REMAIN-1 study, including participant follow-up through 52 weeks. If our De Novo request is granted, we believe longer-term follow-up studies beyond 52 weeks will likely be performed as part of a post-market study, which may include studying the safety and effectiveness of repeat procedures, should they be necessary. Based on regulatory precedent, we believe such post-market studies may be conducted in parallel with the commercial launch of Revita. If our De Novo request is granted, 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 procedural therapy alternative to ongoing maintenance use of GLP-1s, and ultimately expand procedure volume as an attempt to validate Revita in endocrine and endoscopy communities as a durable and potentially repeatable option for patients living with obesity, prediabetes and other metabolic diseases.

As we progress our Revita clinical program and generate clinical evidence in support of Revita, we will invest in building a U.S. based direct sales force to support our U.S. launch to prepare for Revita's potential FDA marketing authorization. We will seek to strategically recruit representatives with strong backgrounds and experience in the management of obesity and metabolic disease, as well as those with a deep understanding of therapeutic GI endoscopy. 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 Revita clinical program, we plan to carry out an organized medical education effort to inform gastroenterologists and endoscopic surgeons around the compelling solution provided by our product candidates, as we believe they will serve as the primary customers for our therapies. We believe that the clinical evidence generated from our program will continue to support our messaging to key leaders in the field of metabolic endoscopy. In parallel, we plan to leverage our LOI with Everself (formerly Bariendo) as this potential partnership will bring a scalable, physician-driven platform designed to deliver metabolic endoscopic solutions at the nation's largest network of high-volume hospital and ambulatory endoscopy centers across the U.S.

If Revita receives marketing authorization, we intend to commercially launch with our next generation commercial console, which has been designed for scalability and ease-of-use. We plan to execute an efficient "hub-and spoke" commercialization strategy to position Revita as a novel procedural therapy to treat obesity and T2D and drive its rapid adoption. Leveraging key learning and insights from our Revita clinical program, we plan to have a targeted sales force initially focusing on centers of excellence with metabolically focused GI endoscopists and surgical endoscopists with a dedicated interest in bariatric and metabolic endoscopy. 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 a focus on patients directly with GI endoscopy suites and practices, as well as direct marketing campaigns to raise awareness amongst patients for a compelling new treatment alternative in weight maintenance and obesity.

We also plan to roll out a robust procedural training and support program for GI and surgical 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 people living with obesity who desire an off-ramp from GLP-1 drugs, and progress to other unmet needs in the treatment and prevention of metabolic diseases, including T2D. Once we are established in obesity and prediabetes 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 metabolic diseases, CVD, and 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 obesity and prediabetes in international markets, we believe there is a significant unmet need for a scalable, disease-modifying therapy globally. We plan to pursue regulatory authorizations, approvals and geographic expansion into international markets with reimbursement and a need for procedure-based solutions in obesity and prediabetes, as part of our long-term growth strategy.

Because Rejuva is designed to leverage the same patient referral pathways, physicians, skill sets and commercialization footprint of Revita, we believe that a successful launch of Revita, if authorized will enable a more rapid commercialization of Rejuva into that same channel, if both products receive marketing authorization in the U.S.

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 1, 2026, our research and development team was comprised of 73 employees. For the years ended December 31, 2025 and 2024, we incurred research and development expenses of approximately \$74.5 million and \$70.5 million, respectively. Major components of the research and development expenses included salaries and benefits, engineering, preclinical and clinical study expenses.

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 obesity, T2D and other metabolic diseases.

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. We also may face competition from companies developing endoscopic and other procedure-based metabolic interventions, including duodenum-targeted therapies. 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 approved or in development for obesity and T2D, such as oral GLP-1s, other nutrient-stimulated hormones and novel mechanisms, which may offer evidence of significant weight loss and broad metabolic benefit. Pharmaceutical companies are heavily invested in their existing and future product platforms for obesity and 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 1, 2026, we own: 36 issued U.S. patents; 34 pending U.S. non provisional patent applications; five pending U.S. provisional patent applications; two patent cooperation treaty (“PCT”), applications that have not entered national stage; 51 issued foreign patents in Australia, Brazil, Canada, China, Europe, Israel, Japan, Korea, and Russia; and 26 pending foreign patent applications in Australia, Canada, China, Europe, Israel, India, Japan, and Korea. Patent counts reflect the patents we maintain. We may allow patents and applications that are not material to our business to lapse. The subject matter covered by our owned patents and patent applications include: Revita and components thereof, methods of using Revita, Rejuva and components thereof, methods of using Rejuva, 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 January 2041; our owned issued foreign patents are expected to expire between January 2032 and October 2040; any patents that may issue from our owned pending U.S. patent applications are expected to expire between January 2032 and February 2047; any patents that may issue from our owned pending foreign patent applications or PCT applications are expected to expire between January 2032 and January 2045.

With respect to Revita, as of March 1, 2026, we own: 34 issued U.S. patents; 27 pending U.S. patent applications; one pending U.S. provisional patent applications; one PCT application that has not entered national stage; 51 issued foreign patents in Australia, Brazil, Canada, China, Europe, Israel, India, Japan, Korea, and Russia; and 17 pending foreign patent applications in Australia, Canada, China, Europe, Israel, 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 July 2046, excluding any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, as applicable.

With respect to Rejuva, as of March 1, 2026, we own: six pending U.S. patent applications; six pending U.S. provisional patent applications; one PCT application that has not entered national stage; and nine pending foreign patent applications in Australia, Canada, China, Europe, Japan and Korea. Any patents that may issue from our pending patent applications related to Rejuva are expected to expire between February 2042 and February 2047, 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 U.S., the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the U.S., 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 1, 2026, we own 44 registered trademarks and three pending trademark applications for FRACTYL, FRACTYL HEALTH, FRACTYL HEALTH LOGO, REVITA, REVITA DMR, REJUVA and other product related brand names in the U.S. 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 Part I, Item 1A, “Risk Factors—Risks Related to Our Intellectual Property.”

Manufacturing and Supply

We currently perform final assembly and acceptance testing of Revita at our headquarters in Burlington, Massachusetts. We rely upon third-party suppliers for the manufacture of sub-assembly components, the sterilization of final components of the Revita system, the device component of the Rejuva product and the Rejuva gene therapy candidates. 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 drug products, 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 U.S., 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 Management System Regulation (“QMSR”), and the FDA’s current good manufacturing practices (“cGMPs”), which cover the methods used in, and the facilities used for, the design, testing, control, manufacturing, sterilization, 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. Our manufacturing operations, and those of our suppliers, are designed to be 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 U.S., as well as comparable authorities in foreign jurisdictions. For example, certain of our product candidates are subject to regulation as medical devices in the U.S. under the Federal Food, Drug, and Cosmetic Act (“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 (“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, record keeping, 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 U.S. requires either FDA clearance of a premarket notification submitted under Section 510(k) of the FDCA, classification under FDA’s *de novo* classification process or approval of a PMA application. 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 QMSR, establishment registration and device listing, reporting of adverse medical events and certain device malfunctions, known as medical device reporting (“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 among other things 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 and is granted upon a determination that the device is substantially equivalent to a legally marketed predicate device. For novel devices that are low to moderate risk but for which no legally marketed predicate device exists, a manufacturer may instead seek marketing authorization through the *De Novo* classification process. If granted, a *De Novo* request results in classification of the device as Class I or Class II and may establish special controls applicable to the device type, after which the device may serve as a predicate for future 510(k) submissions. Devices deemed by the FDA to pose the greatest risks, such as life-sustaining, life-supporting or certain implantable devices, or devices that present risks that cannot be adequately controlled through general and special controls, are placed in Class III and generally require approval of a PMA prior to commercialization. Some pre-amendment devices remain unclassified but are subject to the FDA’s premarket notification and clearance requirements 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.

De Novo Classification Pathway

The De Novo classification process is a marketing pathway for novel medical devices that are low to moderate risk and for which there is no legally marketed predicate device. A manufacturer may submit a De Novo request directly if no appropriate predicate exists, or after receiving a "not substantially equivalent" determination in response to a 510(k) submission. In a De Novo request, the manufacturer must provide sufficient information to demonstrate reasonable assurance of safety and effectiveness for the device's intended use and to show that general controls alone, or general and special controls, are adequate to mitigate identified risks. Submissions typically include a detailed device description, nonclinical performance testing, risk analysis, proposed labeling, and, where necessary, clinical data.

Based on clinical safety data generated to date and provided to the FDA, the FDA has indicated that Revita may be appropriate for classification as a Class II device, and we intend to seek a De Novo classification order from the FDA as our pathway to marketing authorization. There can be no assurance, however, that the FDA will grant the De Novo request, that the FDA will not require additional information or clinical data before completing its review, or that unforeseen safety events arising from our ongoing clinical studies will not cause the FDA to reassess Revita's risk classification. If the FDA determines that safety events identified during the REMAIN-1 study or otherwise warrant reclassification to Class III, we may be required to pursue PMA approval rather than De Novo classification, which would significantly increase the time, cost, and data requirements necessary to obtain marketing authorization. See "—PMA Approval Pathway" below.

Following submission, the FDA conducts an acceptance review and substantive review of the De Novo request. Although the statute provides the FDA with 150 review days, the total review timeline is often longer due to requests for additional information and sponsor response time. De Novo submissions are subject to user fees, which are generally higher than 510(k) fees but lower than PMA fees. If the FDA grants the De Novo request, the device is classified as Class I or Class II, and the FDA may establish special controls necessary to provide reasonable assurance of safety and effectiveness. The granted De Novo classification creates a new device type that may serve as a predicate for future 510(k) submissions.

After a device receives a De Novo classification, the manufacturer is subject to general medical device regulatory requirements, including establishment registration and device listing, QMSR compliance, medical device reporting, labeling requirements, and other post-market controls. Unlike PMA-approved devices, De Novo-classified devices are not subject to routine annual reporting requirements, although the FDA may impose post-market surveillance requirements as special controls or conditions of the classification order. Modifications that could significantly affect the safety or effectiveness of the device, or that constitute a major change in intended use, may require submission of a new 510(k), a new De Novo request, or a PMA, and the FDA may take enforcement action if it determines that a required marketing authorization was not obtained.

PMA Approval Pathway

Although we are currently pursuing De Novo classification for Revita based on the FDA's assessment of Revita as a Class II device, we may be required to seek PMA approval if the FDA determines, based on unforeseen safety events arising from the REMAIN-1 study or other ongoing clinical activities, that Revita poses risks inconsistent with Class II designation and should be reclassified as a Class III device. A Class III device requires PMA approval before it can be commercially marketed. The PMA process is substantially more demanding than the De Novo classification process and would significantly extend the time and resources required to obtain marketing authorization for Revita.

In a PMA, the manufacturer must demonstrate that the device is safe and effective, supported by extensive 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 application, the FDA determines whether the application is sufficiently complete to permit substantive review. If the FDA accepts the application for review, it has 180 days under the FDCA to complete its review,

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 regarding approvability. The FDA may or may not accept the panel's recommendation. The FDA will generally conduct a pre-approval inspection of the applicant's or its third-party manufacturers' or suppliers' manufacturing facility or facilities to ensure compliance with the QMSR. PMA applications are also subject to user fees, which are higher than those applicable to De Novo submissions.

The FDA will approve a 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. The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including restrictions on labeling, promotion, sale, and distribution, and requirements to collect long-term follow-up data from clinical study participants or to conduct additional post-approval studies. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of 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 or a *de novo* request, and are sometimes required to support a 510(k) submission. All clinical investigations of devices conducted in the U.S. to determine safety and effectiveness must be conducted in accordance with the FDA's IDE regulations which among other things govern investigational device labeling, prohibit promotion of the investigational device, and specify an array of record keeping, 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 ("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 participants, as approved by the FDA. If the device presents a non-significant risk to the participant, 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 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 participant informed consent, rigorously follow the investigational plan and study protocol, control the disposition of the investigational device, and comply with all reporting and record keeping 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 QMSR, which currently 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;

- complying with the laws and regulations requiring Unique Device Identifiers on commercialized devices and also requiring the submission of certain information about each device to the FDA's Global Unique Device Identification Database;
- 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 QMSR, which currently 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 QMSR also requires, among other things, maintenance of a device master file, device history file, and complaint files. Manufacturers of medical devices are subject to periodic scheduled and unscheduled inspections by the FDA. Failure to maintain compliance with the QMSR 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 marketing authorization, 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 Federal Trade Commission 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 U.S., which can change rapidly with relatively short notice.

United States Regulation of Biologics and Combination Biologic/Device Products

In the U.S., 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 U.S. 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 ("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 U.S. generally involves the following:

- completion of certain preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements ("GLPs");
- submission to the FDA of an 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 ("GCPs");
- preparation of and submission to the FDA of a BLA;
- 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 QMSR 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,
- satisfactory completion of potential FDA inspection 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 U.S.

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 for certain *in vivo* studies.

Prior to beginning the first clinical trial with a product candidate in the U.S., 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.

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 to the IND submission process, under the National Institutes of Health ("NIH"), Guidelines for Research Involving Recombinant DNA Molecules ("NIH Guidelines"), supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee ("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 among other things, 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.
- 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 labeling.

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 within the approved indication. These so-called Phase 4 studies may also be made a condition to approval of the BLA.

In addition, during the development of a biologic product candidate, 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.

Concurrent with clinical trials, sponsors 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, including results from 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.

In addition, the Pediatric Research Equity Act ("PREA"), requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, BLAs and certain supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is deemed safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

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 a period of three months for FDA to respond to information deemed a "major amendment" to the application.

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. During its review of the application, 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.

After the FDA evaluates a BLA and conducts any required 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 ("CRL"). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will generally 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 ("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 post-market studies and surveillance programs 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 application 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.

Certain investigational biologics may also be eligible for regenerative medicine advanced therapy (“RMAT”), designation. This designation may be available where the product candidate qualifies as an RMAT, meaning that, with limited exceptions, the investigational drug: (1) is a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products; (2) is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such a disease or condition. The RMAT designation provides all the benefits of a breakthrough therapy designation, including more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review of a BLA submission. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, as discussed below, or through reliance upon data obtained from a meaningful number of clinical trial sites, including through expansion of trials to additional sites.

Any marketing application for a biologic product candidate submitted to the FDA for approval, including a product candidate with a fast track designation, RMAT 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. 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, depending on the design of the applicable clinical studies, 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 confirmatory clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. The FDA may require, that such confirmatory studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under the FDORA, the FDA has increased authority for expedited procedures to withdraw approval of the product receiving accelerated approval if the sponsor fails to conduct the required post-marketing studies in a timely manner or if such studies fail to verify the predicted clinical benefit. In addition, the FDA 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, RMAT 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 ("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 U.S. 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 existing 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 (“Medical Devices Directive”), which has been repealed and replaced by Regulation (EU) No 2017/745 (“Medical Devices Regulation”). In accordance with the Medical Devices Regulation’s recently extended transitional provisions, both (i) devices lawfully placed on the market pursuant to the Medical Devices Directive prior to May 26, 2021, and (ii) legacy devices lawfully placed on the EU market after May 26, 2021 in accordance with the Medical Devices Regulation transitional provisions may generally continue to be made available on the market or put into service, provided that the requirements of the transitional provisions are fulfilled. However, even in this case, manufacturers must comply with a number of new or reinforced requirements set forth in the Medical Devices Regulation with regard to registration of economic operators and of devices, post-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.

In the EU, there is currently no premarket government review of medical devices. However, the EU requires that, all medical devices placed on the market in the EU must meet the safety and performance requirements laid down in Annex I to the Medical Devices Regulation, including the requirement that a medical device must be designed and manufactured in such a way that during normal conditions of use, it is suitable for its intended purpose. Medical devices must be safe and effective and must not compromise the clinical condition or safety of patients, or the safety and health of users and – where applicable – other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 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 general safety performance requirements as a practical matter as it creates a rebuttable presumption that the device satisfies that essential requirement general safety and performance.

Compliance with the general safety and performance requirements of the Medical Devices Regulation is a prerequisite for European conformity marking (“CE mark”), without which medical devices cannot be marketed or sold in the EU. To demonstrate compliance with the general safety and performance 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 general safety and performance 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 issue an EU declaration of conformity based on a self-assessment of the conformity of its products with the general safety and performance 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 manufacturer's 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 general safety and performance 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 EC 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).

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 Medical Devices 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 ("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 ("UDI-DI"), specific to the manufacturer and the device, and a production identifier ("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. Certain obligations for registration in EUDAMED are expected to become applicable in Q1 2026 (as EUDAMED is not yet fully functional). Until EUDAMED is fully functional, the corresponding provisions of the Medical Devices Directive continue to apply for the purpose of meeting the obligations laid down in the provisions regarding exchange of information, including, and in particular, information regarding registration of devices and economic operators.

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 ("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. Manufacturers are required to take FSCAs, which are 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. A serious incident is any malfunction or deterioration in the characteristics or performance of a device on the market (e.g., inadequacy in the information supplied by the manufacturer, undesirable side-effect), which, might lead to either the death or serious deterioration of the health of a patient, user, or other persons, or to a serious public health threat. 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 ("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 (“EEA”), which consists of the 27 EU Member States plus Norway, Liechtenstein and Iceland.

Brexit and the Regulation of Medical Devices in the United Kingdom

From January 1, 2021 onwards, the Medicines and Healthcare products Regulatory Agency (“MHRA”), has been the sovereign regulatory authority responsible for the Great Britain (“GB”) (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), or UK Medical Devices Regulations, 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 transition period on January 1, 2021, new regulations require medical devices to be registered with the MHRA before being placed on the GB market. The MHRA will only register devices where the manufacturer or their United Kingdom (“UK”), Responsible Person has a registered place of business in the UK. Manufacturers based outside the UK need to appoint a UK Responsible Person that has a registered place of business in the UK to register devices with the MHRA. Furthermore, on December 16, 2024, the UK government published an amendment to the UK Medical Devices Regulations to clarify and strengthen the post-market surveillance requirements for medical devices in GB. This amendment will come into force on June 16, 2025 and aims to facilitate greater traceability of incidents and trends enabling the MHRA to act swiftly when needed to address safety issues and support the entire health system in better protecting patients. In addition, the MHRA launched a consultation between November 14, 2024 and January 5, 2025 on proposals to update the pre-market requirements for medical devices in GB, covering four topics, namely: (1) a new international reliance scheme to enable swifter market access for certain devices that have already been approved in a comparable regulator country; (2) the UKCA mark and, in particular, proposals to remove the requirement to place such UKCA mark on devices; (3) conformity assessment procedures for in vitro diagnostic devices; and (4) maintaining in UK law certain pieces of “assimilated” EU law which are due to sunset in 2025. This consultation builds on the MHRA’s previous consultation between September and November 2021, and the UK government’s response to that consultation which was published on June 26, 2022. The MHRA has stated that it will incorporate feedback to its recent consultation into new legislation on pre-market requirements for medical devices in GB. The new legislation is expected to be implemented in 2026 and aims to enable greater international collaboration and practices, with more patient-centered, proportionate requirements for medical devices which are responsive to technological advances.

Under the UK Medical Devices Regulations, certain medical devices need to be “UKCA” certified by a UK approved body in order to be lawfully placed on the GB market. However, certain medical devices in compliance with: (1) the (EU) Medical Devices Directive can continue to be placed on the GB market until the sooner of certificate expiration or June 30, 2028 or (2) the (EU) Medical Devices Regulation can continue to be placed on the GB market until the sooner of certificate expiration or June 30, 2030.

In addition, the Trade and Cooperation Agreement (“TCA”), between the UK 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 U.S., 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 U.S., including the EU, require that CTAs, 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 U.S. 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 U.S., 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 (pharmaco-toxicological) studies must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). GLP principles define a set of rules and criteria for a quality system concerned with the organizational process and the conditions under which these non-clinical studies are planned, performed, monitored, recorded, archived and reported. 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 Council on Harmonization, of Technical Requirements for Pharmaceuticals for Human Use (“ICH”), guidelines on good clinical practices (“GCP”), as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products (“ATMPs”). 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 member states, the sponsor is liable to provide ‘no fault’ compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation (“CTR”), which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the EU Clinical Trials Directive required a separate CTA to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. 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. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state’s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR transition period ended on January 31, 2025, and all clinical trials and related applications are now fully subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

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 (“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 (“MAA”). The process for doing this depends, among other things, on the nature of the medicinal product.

There are two types of MAs:

- “Centralized MAs” are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use (“CHMP”), of the European Medicines Agency (“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) 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 (“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 (“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.

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 “standard” 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.

MAAs 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.

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 U.S., 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 the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (“PSURs”).

All new MAAs must include a risk management plan, 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 and the Regulation of Medicinal Products in the United Kingdom

The TCA, agreed between the UK and the EU has been 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 of GMP inspections of manufacturing facilities for medicinal products and GMP 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 UK and EU and also grants each of the UK 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) will not be applicable in GB. The Medicines and Medical Devices Act 2021 has introduced 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 applied in Northern Ireland than in GB (i.e., England, Wales, and Scotland); broadly, Northern Ireland continued to follow the EU regulatory regime. However, on January 1, 2025, a new arrangement called the “Windsor Framework” came into effect and reintegrated Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products. The Windsor Framework removes EU licensing processes, and EU labeling and serialization requirements in relation to Northern Ireland, and introduces a UK-wide licensing process for medicinal products.

MAs in the UK are governed by the Human Medicines Regulations (SI 2012/1916), as amended. 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 chose to opt-out. Under the terms of the Windsor Framework, these MAs became valid for the whole of the UK from January 1, 2025. In order to use the EU centralized procedure to obtain an MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore, since Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures. Applications are governed by the Human Medicines Regulations (SI 2012/1916), as amended, and are made electronically through the MHRA Submissions Portal. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicinal products that will benefit patients, including a 150-day assessment (subject to clock-stops) and a rolling review procedure. In addition, an international recognition procedure (“IRP”), has been in place since January 1, 2024, whereby the MHRA will have regard to decisions on the approval of MAs

made by the EMA and certain other regulators when determining an application for a new UK MA. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (i.e., the regulators in Australia, Canada, Switzerland, Singapore, Japan, the U.S. and the EU). The MHRA will conduct a targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. The IRP allows medicinal products approved by such trusted regulatory partners that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update an MA in the UK. Applications should be decided within a maximum of 60 days if there are no major objections identified that cannot be resolved within such 60-day period and the approval from the trusted regulatory partner selected has been granted within the previous 2 years, or if there are such major objections identified or such approval has not been granted within the previous 2 years within 110 days. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals. In the UK, the initial duration of an MA is five years and following renewal will be valid for an unlimited period unless the MHRA decides on justified grounds relating to pharmacovigilance, to proceed with only one additional 5-year renewal. Any authorization which is not followed by the actual placing of the medicinal product on the market in the UK within 3 years shall cease to be in force.

There is no pre-MA orphan designation in the UK. Instead, the MHRA reviews 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 the UK, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in the UK.

Coverage and Reimbursement in Foreign Countries

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 member states in the EU, do not follow price structures of the U.S. and prices generally tend to be significantly lower.

Other Healthcare Laws

Healthcare Fraud and Abuse Laws

In the U.S., 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. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, 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 False Claims Act or federal civil monetary penalties. 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. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. 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 (“HIPAA”), 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.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information and their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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 CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers (such as physician assistants and nurse practitioners), and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician’s immediate family members.

Federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products.

Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Some state and local laws require certain regulatory licenses to manufacture or distribute our products commercially and/or the registration of medical device and/or pharmaceutical sales representatives in the jurisdiction. Many U.S. states have adopted laws similar to the

federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require manufacturers to implement compliance programs or to comply with the pharmaceutical and medical device industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government. Several states also impose other marketing restrictions or require manufacturers to make marketing or price disclosures to the state. State and foreign laws, including, for example, the European Union General Data Protection Regulation, which became effective May 2018, also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Violations of fraud and abuse laws, including federal and state anti-kickback and false claims laws, may be punishable by significant criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), curtailment or restructuring of operations, 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.

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 and 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 U.S., on manufacturers. Certain countries also mandate implementation of commercial compliance programs.

Coverage and Reimbursement in the United States

Significant uncertainty exists as to the coverage and reimbursement status of procedures using any product candidates for which we may obtain regulatory approvals. In the U.S., 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 U.S., 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 U.S., 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. In the U.S., the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and certain private payors may follow CMS policies. 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 U.S. 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.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

There has also been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. For example, HHS imposes rebates on many Medicare Part B and Medicare Part D products to penalize price increases that outpace inflation on an annual basis. In addition, HHS has been empowered to negotiate the price of certain single-source biologics that have been on the market for at least eleven (11) years covered under Medicare as part of the Medicare Drug Price Negotiation Program. Each year up to twenty (20) products will be selected by HHS for the Medicare Drug Price Negotiation Program. Products subject to the Medicare Drug Price Negotiation Program are expected to experience a significant reduction in reimbursement from the Medicare program on a per unit basis.

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, 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. Historically, products launched in the EU do not follow the price structures of the United States and product prices in the EU have generally been significantly lower as compared to the U.S.

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 U.S. 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 U.S. 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 U.S. 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 and executive actions 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, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively the “ACA”), in the U.S., for example, has changed healthcare financing and delivery by both governmental and private insurers substantially, and affected medical device manufacturers significantly.

Since its enactment, there have been judicial, executive and political challenges to certain aspects of the ACA. For example, on July 4, 2025, the One Big Beautiful Bill Act (the “OBBBA”) was signed into law, which narrowed access to ACA marketplace exchange enrollment and declined to extend the ACA enhanced advanced premium tax credits that expired at the end of 2025, which, among other provisions in the law, are anticipated to reduce the number of Americans with health insurance. The OBBBA also is expected to reduce Medicaid spending and enrollment by implementing work requirements for some beneficiaries, capping state-directed payments, reducing federal funding, and limiting provider taxes used to fund the program. Congress is considering proposed legislation intended to further reduce healthcare costs with alternatives to replace the expired ACA subsidies. 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:

- 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 2032, 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.
- The American Rescue Plan Act of 2021 eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug’s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

The current administration is pursuing policies to reduce regulations and expenditures across government agencies including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. For example, the current administration has announced agreements with pharmaceutical companies that require the drug manufacturers to offer, through a direct-to-consumer platform (TrumpRx), U.S. patients and Medicaid programs prescription drug Most-Favored Nation pricing equal to or lower than those paid in other developed nations, with additional mandates for direct-to-patient discounts and repatriation of foreign revenues. Other recent actions, for example, include (1) directing agencies to reduce agency workforce and cut programs; (2) directing HHS and other agencies to lower prescription drug costs through a variety of initiatives; (3) imposing tariffs on imported pharmaceutical products; and (4) as part of the Make America Healthy Again Commission’s Strategy Report released in September 2025, working across government agencies to increase enforcement on direct-to-consumer pharmaceutical advertising. Additionally, the current

administration recently called on Congress to enact “The Great Healthcare Plan,” to codify and expand Most-Favored Nation pricing, lower government subsidies to private insurance companies, increase healthcare price transparency, expand pharmaceutical drugs available for over-the-counter purchase, and enact restrictions on pharmacy benefit manager payment methodologies, among other things. These actions and policies may significantly reduce U.S. drug prices, potentially impacting manufacturers’ global pricing strategies and profitability, while increasing their operational costs and compliance risks. In June 2024, in *Loper Bright Enterprises v. Raimondo*, the U.S. Supreme Court greatly reduced judicial deference to regulatory agencies, which could increase successful legal challenges to federal regulations affecting our operations. Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment (“HTA”), amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product, i.e., oncology and advanced therapy medicinal products as of 2025, certain high-risk medical devices as of 2026, orphan medicinal products as of 2028, and all other medicinal products by 2030. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect additional state, federal and foreign 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.

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 U.S., 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 European Union’s General Data Protection Regulation (“EU GDPR”), the United Kingdom’s GDPR (“UK GDPR”) (collectively, “GDPR”) imposes strict requirements for processing the personal data of individuals within the European Economic Area and United Kingdom. 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 Euros under the EU GDPR, 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. 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 may lead to significant civil and/or criminal penalties and restrictions on data processing.

Employees and Human Capital Resources

On January 31, 2025, we announced that pursuant to our Strategic Reprioritization, we streamlined resources, including a workforce reduction impacting 22 employees, or approximately 17% of our workforce. The Strategic Reprioritization was substantially implemented by the second quarter of 2025. As of March 1, 2026, we have 100 full-time employees, 73 of whom are dedicated to research and development, and 14 of whom 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 recognize that our continued ability to attract, retain and motivate exceptional employees is vital to ensuring our long-term competitive advantage. Our employees are critical to our long-term success and are essential to helping us meet our goals. Among other things, we support and incentivize our employees in the following ways:

- ***Talent Development, Compensation and Retention.*** We strive to provide our employees with a rewarding work environment, including the opportunity for growth, success and professional development. 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—all designed to attract and retain a skilled and diverse workforce.
- ***Health and Safety.*** We support the health and safety of our employees by providing health care, retirement planning, paid time off and other additional benefits, which are intended to assist employees to manage their well-being.

Corporate Information

Fractyl Health, Inc. was originally incorporated in Delaware on August 30, 2010 under the name MedCatalyst, Inc. The Company subsequently changed its name to Fractyl Laboratories Inc. on January 10, 2012 and then to Fractyl Health, Inc. on June 9, 2021.

Available Information

We file electronically with the U.S. Securities and Exchange Commission (the “SEC”) our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements and other information. Our filings with the SEC are available to the public over the Internet at the SEC’s website at www.sec.gov. We make available on our website at <http://ir.fractyl.com>, free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC. The information on our website is deemed not to be incorporated in this Annual Report on Form 10-K or to be part of this Annual Report on Form 10-K.

Item 1A. Risk Factors.

You should carefully consider the risks and uncertainties described below and the other information in this Annual Report on Form 10-K, including our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K and in Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations. Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. See "Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain important 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 which have received marketing authorization 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 a 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 U.S. and have not generated any revenue from product sales. We received CE mark for Revita in Europe, following its European Certification in 2016, and have received reimbursement authorization through NUB in Germany for the treatment of T2D. 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 lead product candidate Revita, including the ongoing REMAIN-1 pivotal clinical study, and preclinical and clinical studies of our product candidate Rejuva. Pursuant to our Strategic Reprioritization, we paused additional investment in our Revita programs for T2D, which consist of the REVITALIZE-1 study and the Germany Real-World Registry study. We are continuing to follow existing participants in both studies per protocol and will report clinical, health economic, and participant-relevant outcomes from the Germany Real-World Registry study on an ongoing basis. We have not yet demonstrated our ability to successfully complete any pivotal clinical studies, submit a De Novo classification request for marketing authorization, or premarket application ("PMA"), a new drug application, or biologic license application ("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, we expect to continue to incur significant net losses for the foreseeable future and may never achieve or sustain profitability, and we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We have incurred net losses since inception, have not generated any significant revenue from product sales to date and have financed our operations primarily through the proceeds from sales of our equity and debt financing. We have incurred a net loss of approximately \$141.0 million and \$68.7 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of approximately \$556.3 million. As noted elsewhere in this Annual Report on Form 10-K, we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. Our losses have resulted principally from expenses incurred in research and development of our product candidates, as well as management and administrative costs and other expenses that we have incurred while building our business infrastructure. Our lead product candidate, Revita, is currently undergoing the REMAIN-1 pivotal clinical study, a randomized, double-blind trial of Revita versus sham in participants who have lost at least 15% total body weight on tirzepatide therapy and wish to discontinue their GLP-1 therapy without weight regain. Pursuant to our Strategic

Reprioritization we paused additional investment in our Revita programs for T2D, which consist of the REVITALIZE-1 study and the Germany Real-World Registry study.

We are continuing to follow existing participants in both studies per protocol and will report clinical, health economic, and participant-relevant outcomes from the Germany Real-World Registry study on an ongoing basis. We expect that it will be several years, if ever, before we have a commercialized product in the U.S. and generate significant revenue from product sales. Even if we succeed in receiving marketing authorization 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 candidates 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 marketing authorization 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 authorization and intend to commercialize;
- expand our manufacturing and develop our commercialization efforts; and
- operate as a public company.

To date, we have generated revenue from our pilot commercial launch of Revita in Germany, in which additional investment has been paused. 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 marketing authorization, and manufacturing, marketing and selling any product candidates for which we may obtain marketing authorization, 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 in the U.S. 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 marketing authorizations, 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.

We require substantial additional capital or must implement other business strategies to execute our operating plan and continue to operate as a going concern. 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 authorization 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 authorization 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. We are incurring additional costs associated with operating as a public company. Accordingly, we will need to obtain additional funding beyond the proceeds from our IPO, ATM Offering, August 2025 Offering, and September 2025 Offering in order to maintain our continuing operations in the future.

As of December 31, 2025, we had approximately \$81.5 million in cash and cash equivalents which will be sufficient to fund our operating expenses and capital expenditure requirements into early 2027, through multiple key clinical and regulatory milestones. Our estimate as to how long we expect our existing cash and cash equivalents to be able to continue to fund our operating expenses and capital expenditure requirements is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. In addition, without additional financing, we may not be able to comply with the minimum liquidity covenant related to our 2023 Notes by the end of 2026.

Given the inherent risk and uncertainty of future cash flow estimates as well as the minimum liquidity covenant requirement, our management has concluded that substantial doubt exists about our ability to continue as a going concern for at least one year after the date that these financial statements are issued. Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock, and it may be more difficult for us to obtain financing. If potential collaborators decline to do business with us or potential investors decline to participate in any future financings due to such concerns, our ability to increase our cash position may be limited.

Our estimate as to how long we expect 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;
- our business strategy, including our Strategic Reprioritization;

- the potential negative impact of 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 authorized, approved (or certified), 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 authorized, approved (or certified);
- 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 authorized, approved (or certified);
- the cost of establishing sales, marketing, and distribution capabilities for any product candidates for which we may receive regulatory authorization, approval (or certification) in regions where we choose to commercialize our products, if authorized, approved (or certified), on our own; and
- the cost of operating as a public company.

We plan to use our existing cash and cash equivalents to fund the ongoing REMAIN-1 pivotal clinical study of Revita; fund the continued preclinical and clinical development of our Rejuva gene therapy candidate RJVA-001; follow the existing participants in the REVITALIZE-1 pivotal clinical study of Revita per protocol, follow the Germany Real-World Registry study participants per protocol and for working capital and other general corporate purposes, including medical education and other commercial readiness activities. Advancing the development of our product candidates will require a significant amount of capital. 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 authorized, approved (or certified).

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 Credit 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 global macroeconomic and geopolitical events 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.

Our Credit Agreement contains restrictive and financial covenants that may limit our operating flexibility.

Our Credit Agreement contains certain restrictive covenants that either limit our ability to, or require a mandatory prepayment in the event that we (i) engage in businesses other than businesses in which we are currently engaged or businesses reasonably related or complementary thereto, or (ii) subject to certain baskets and exceptions, incur additional indebtedness or liens, make certain investments, make certain payments of indebtedness, pay dividends or make any other distributions, merge with other companies or consummate certain changes of control, acquire other companies, transfer or dispose of certain assets, and enter into transactions with affiliates, among other things. We therefore may not be able to engage in any of the foregoing transactions unless we obtain the consent of all or a majority of the lenders under the Credit Agreement or prepay our outstanding obligations under the Credit Agreement. The Credit Agreement contains financial covenants including a minimum liquidity covenant requiring us to maintain a minimum \$10.0 million balance in cash and

cash equivalents on deposit in accounts, subject to certain exceptions. We may not be able to maintain the minimum liquidity covenant related to the Credit Agreement without additional financing. Our obligations under the Credit Agreement are collateralized by substantially all of our assets, including our intellectual property, but excluding certain customary and agreed upon assets. Additionally, we may not be able to generate sufficient cash flow or sales to pay the principal and interest under the Credit Agreement. Furthermore, our future working capital, borrowings or equity financings could be unavailable to repay or refinance the amounts outstanding under the Credit Agreement. In the event of a liquidation, the lenders and the agent under the Credit Agreement would be repaid all outstanding principal and interest prior to distribution of assets to unsecured creditors, and the holders of our common stock would receive a portion of any liquidation proceeds only if all of our creditors then existing, including the agent and lenders under the Credit Agreement, were first repaid in full. See “—We require substantial additional capital or must implement other business strategies to execute our operating plan and continue to operate as a going concern. 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.”

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 will be required to obtain further funding through a variety of means, including through public or private equity offerings, debt financings, including our Credit Agreement, 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.

Unfavorable global economic conditions, including any adverse macroeconomic conditions or geopolitical events, including the conflict between Ukraine and Russia, the conflict between Israel and Hamas, the conflict between Iran and the U.S. and recent bank failures affecting the financial services industry, have affected and could further adversely affect our business, financial condition, results of operations or liquidity, either directly or through adverse impacts on certain of the third parties on which we rely to conduct certain aspects of our preclinical studies or clinical studies.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Global economic and business activities continue to face widespread uncertainties, and global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, rising inflation and monetary supply shifts, rising interest rates, tariffs, labor shortages, declines in consumer confidence, declines in economic growth, increases in unemployment rates, recession risks, and uncertainty about economic and geopolitical stability. Additionally, changing trade policies and geopolitical disputes and other international conflicts have resulted in increased tariffs, sanctions and other measures that restrict international trade, and may materially adversely affect our business, particularly if these measures affect regions where manufacturing and product development activities take place or raw materials are sourced. For example, tensions between the U.S. and other countries have led to a series of tariffs being imposed by the U.S. and those countries, as well as other business restrictions. Countries may also adopt other measures, such as controls on imports or exports of goods, technology or data, that could adversely impact our operations and supply chain. As these tensions continue to rise, more targeted approaches on certain products, industries or companies could significantly impact our development and commercialization efforts. The U.S. government has recently imposed tariffs on certain foreign goods, and some foreign governments have threatened or instituted retaliatory tariffs on certain U.S. goods and have indicated a willingness to impose additional tariffs on U.S. products, which could increase the cost of goods needed to commercialize our products and continue development of our product candidates. Our current third-party drug product suppliers and manufacturers with whom we may experience supply chain disruptions as a result of increased costs and uncertainty, including risks to their long-term viability, which may impact our ability to meet customer demand or cause reputational harm if we are unable to deliver our products on expected timelines. Further, such actions by the U.S. could result in other retaliatory actions by those countries which could impact our ability to profitably commercialize our products in those jurisdictions. As a result, our business, operations, and financial condition could be materially harmed.

A severe or prolonged economic downturn, or additional global financial or political crises, could result in a variety of risks to our business, including delayed clinical studies or preclinical studies, delayed authorization, approval (or certification) of our product candidates, delayed ability to obtain patents and other intellectual property protection, weakened demand for our product candidates, if authorized, approved (or certified), or our ability to raise additional capital when needed on acceptable terms, if at all. The extent of the impact of these conditions on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected timeframe, as well as that of third parties upon whom we rely, will depend on future developments which are uncertain and cannot be predicted. A weak or declining economy also could strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (“FDIC”), as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership, and on May 1, 2023, First Republic Bank was also swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of Silicon Valley Bank would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under Credit Agreements, letters of credit and certain other financial instruments with Silicon Valley Bank, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. If any of the banks which hold our cash deposits were to be placed into receivership, we may be unable to access such funds. As of December 31, 2025, substantially all of our cash on deposit was maintained at two financial institutions in the U.S., and our current deposits are in excess of federally insured limits. If further failures in financial institutions occur where we hold deposits, we could experience additional risk. Any such loss or limitation on our cash, cash equivalents and short-term investments would adversely affect our business. In addition, if any of the third parties on which we rely to conduct certain aspects of our preclinical studies or clinical trials are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties’ ability to fulfill their obligations to us could be adversely affected.

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, 2025, we had U.S. federal and state net operating loss carryforwards of approximately \$374.1 million and \$329.5 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 (the “Tax Act”), as modified by the Coronavirus Aid, Relief, and Economic Security (“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, 2025, we had U.S. federal and state research and development tax credit carryforwards of \$17.4 million and \$5.3 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 our IPO, together with other transactions that have occurred since our inception, may have triggered such an ownership change pursuant to Section 382. We may have experienced or 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 processes of the FDA, comparable foreign regulatory authorities, and notified bodies is lengthy, time-consuming, and inherently unpredictable, and even if we complete the necessary clinical studies we cannot predict when, or if, we will obtain marketing authorization for any of our product candidates, and any such authorization 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 U.S. We are currently in clinical-stage development of Revita, which is an investigational medical device, and are conducting preclinical and expect to initiate clinical development of our Rejuva candidate RJVA-001 along with a device delivery system, which together with the gene therapy candidate, we anticipate will be regulated as a combination biologic-device in the U.S.

In the U.S., before we can market a new medical device, we must first receive either 510(k) clearance, a De Novo classification order, or PMA approval from the FDA under the FDCA, unless an exemption applies. Based on clinical safety data generated to date and provided to the FDA, FDA has indicated that Revita is appropriate for classification as a Class II device. Accordingly, we intend to seek a De Novo classification order from the FDA as our pathway to marketing authorization for Revita. The De Novo classification process requires that we demonstrate reasonable assurance of safety and effectiveness for Revita's intended use, and that general controls alone, or general and special controls, are adequate to mitigate identified risks. There can be no assurance, however, that the FDA will grant a De Novo classification order, that the FDA will not require additional information or clinical data before completing its review, or that unforeseen safety events arising from our ongoing clinical studies will not cause the FDA to reassess Revita's risk classification.

If the FDA determines, based on safety events identified during the REMAIN-1 study or otherwise, that Revita poses risks inconsistent with Class II designation and should be reclassified as a Class III device, we may be required to pursue PMA approval rather than De Novo classification. The PMA process is typically required for devices deemed to pose the greatest risk, such as life-sustaining, life-supporting, or implantable devices, and is substantially more demanding than the De Novo classification process. In the PMA process, the FDA must determine that a proposed device is safe and effective for its intended use based, in part, on extensive technical, preclinical, clinical, manufacturing, and labeling data. 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. Any such reclassification would significantly increase the time, cost, and data requirements necessary to obtain marketing authorization for Revita and could materially harm our business.

Regardless of the pathway pursued, the authorization process can be expensive, lengthy, and uncertain. Modifications to a device following a De Novo classification order that could significantly affect safety or effectiveness, or that constitute a major change in intended use, may require submission of a new 510(k), a new De Novo request, or a PMA. Any delay or failure to obtain necessary marketing authorization could harm our business. Furthermore, even if marketing authorization is granted, it may include significant limitations on the indicated uses for the device, which may limit the market for Revita.

Similarly, we are not permitted to market any biological product in the U.S. or in foreign jurisdictions until we receive approval of a BLA from the FDA or approval of similar foreign applications from comparable foreign authorities. We anticipate that each of our Rejuva gene therapy candidates 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 applications to comparable foreign authorities. A BLA and similar applications must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety, purity and potency (or efficacy) 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 ("EU"), our products must comply with the general safety and performance requirements of the Medical Devices Regulation ("MDR") (Regulation (EU) No 2017/745), which repeals and replaces the Medical Devices Directive (the "MDD"). Compliance with these requirements is a prerequisite to be able to affix the European conformity ("CE" or "CE mark") to our products, without which they cannot be sold or marketed in the EU. All medical devices placed on the market in the EU must meet the general safety and performance requirements laid down in Annex I to the MDR, including the requirement that a medical device must be designed and manufactured in such a way that, during normal conditions of use, it is suitable for its intended purpose.

Medical devices must be safe and effective and must not compromise the clinical condition or safety of patients, or the safety and health of users and – where applicable – other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 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. Notified bodies are independent organizations designated by EU member states to assess the conformity of devices before being placed on the market. The notified body would typically audit and examine the technical file and the manufacturer’s quality system (notified bodies must presume that quality systems which implement the relevant harmonized standards—ISO 13485:2016 for Quality Management Systems—conform to these requirements), design and final inspection of our devices. If satisfied that the relevant product conforms to the relevant general safety and performance requirements, the notified body issues an EU certificate, 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. If we fail to comply with applicable laws and regulations, we would be unable to affix the CE mark to our products, which would prevent us from selling them within the EU. See Part I, Item 1. Business—Government Regulation—Regulation of Medical Devices in the European Union for more information.

The CE mark for Revita was applied under the MDD, which has now been superseded by the MDR and we are currently working on obtaining MDR certification. Under the recently extended MDR transitional provisions, both (i) devices lawfully placed on the market pursuant to the MDD prior to May 26, 2021 and (ii) legacy devices lawfully placed on the market after May 26, 2021, in accordance with the transitional provisions of the MDR, may generally continue to be made available on the market or put into service, provided that the requirements of the transitional provisions are fulfilled. In particular, no substantial change must be made to the device as such a modification would trigger the obligation to obtain a new certification under the MDR and therefore to have a notified body conducting a new conformity assessment of the devices. Once our devices are certified under the MDR, 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 MDR 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 MDR. If the assessment is favorable, the notified body will issue a new certificate 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 MDR. The notified body may disagree with our proposed changes and product introductions or modifications could be delayed or canceled, which could adversely affect our ability to grow our business.

The aforementioned EU rules are generally applicable in the European Economic Area (“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. We cannot be certain that transitioning towards the MDR will not have any material impact on our sales in the EU and EEA and, if we were considered noncompliant and unable to sell our products in the EU and EEA, 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 the EU have diverged. Northern Ireland has adopted a hybrid approach as a result of the divergence in accordance with the Northern Ireland Protocol. GB’s national legislation remains based on the (EU) MDD as implemented nationally. However, on December 16, 2024, the UK government published an amendment to the UK Medical Devices Regulations to clarify and strengthen the post-market surveillance requirements for medical devices in GB. This amendment will come into force on June 16, 2025. In addition, the Medicines and Healthcare products Regulatory Agency (the “MHRA”) launched a consultation between November 14, 2024 and January 5, 2025 on proposals to update the pre-market requirements for medical devices in GB. The MHRA has stated that it will incorporate feedback to this consultation into new UK legislation on pre-market requirements for medical devices in GB. The new legislation is expected to come into force in 2026. Under the UK Medical Devices Regulations, certain medical devices need to be “UKCA” certified by a UK approved body in order to be lawfully placed on the GB market. However, certain medical devices in compliance with: (1) the (EU) MDD can continue to be placed on the GB market until the sooner of certificate expiration or June 30, 2028. or (2) the (EU) MDR can continue to be placed on the GB market until the sooner of certificate expiration or June 30, 2030. Medical devices also need to bear a physical United Kingdom Conformity Assessment (“UKCA”) mark in order to be

lawfully placed on the GB market. However, one of the key topics in the MHRA's recent consultation was to obtain feedback on whether to remove the requirement for a medical device and its labeling (i.e., packaging and instructions for use) in GB to bear a physical UKCA mark. Instead of requiring a medical device and its labeling to bear a UKCA mark, manufacturers would be required to assign a unique design identification ("UDI"), to medical devices before they are placed on the GB market. If this change is implemented, we may no longer be required to affix the physical UKCA mark to our devices, but we may need to assign and affix a UDI.

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, pure, potent and/or 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 results from clinical studies to meet the level of statistical significance or otherwise demonstrate the evidence 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 submission of a 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 any such 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.

In addition, the FDA and comparable foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products

(potentially reducing the duration of regulatory data protection, revising eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the biopharmaceutical industry in the long term.

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, or with respect to biological product candidates, that such candidates are safe, pure, and potent for their intended 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 participants 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 alignment with the FDA or other regulatory authorities as to the design or implementation of our clinical studies;
- delays in or failure to obtain regulatory allowance or approval to commence a clinical study;
- delays in or failure to reach an agreement on acceptable terms with clinical study sites or prospective 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 participants to participate in a clinical study;
- delays in or failure to have participants 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 clinical studies in accordance with the FDA's good clinical practice ("GCP"), requirements, or applicable regulatory guidelines in other countries;
- failure in addressing participant 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.

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 (“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 U.S. and EU. We could also in the future plan to conduct one or more future clinical studies of our product candidates outside the U.S., including in Europe and Australia. The acceptance of study data from clinical studies conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authorities or notified bodies may be subject to certain conditions or may not be accepted at all. In cases where data from clinical studies conducted outside the U.S. are intended to serve as the sole basis for marketing authorization in the U.S., regardless of whether such clinical studies were conducted pursuant to an IND or IDE, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. 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, if the applicable clinical studies were not otherwise subject to an IND or IDE, the FDA will not accept

the data as support for an application for regulatory approval unless the study was well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. 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 or notified body will accept data from studies conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable regulatory authority or notified body 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 submit 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 in the U.S., if necessary to support for a PMA, 510(k) premarket notification or de novo classification request, a sponsor must, among other things, apply for and obtain institutional review board (“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 U.S. for future devices we develop and intend to market in the U.S. 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. Similar requirements may apply in jurisdictions outside the U.S.

While we plan to submit IDEs or comparable documents for Revita, we may not be able to submit or obtain approval of such IDEs or comparable documents on the timeline we expect. 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;
- the report of prior investigations or the investigational plan;

- the methods, facilities, and controls used for the manufacturing, processing, packaging, storage, and, where appropriate, installation of the device; or
- 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 an 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 we 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. In addition, even if we are able to obtain approval of an IDE, such approval does not guarantee that the applicable clinical investigation, even if successful, will eventually lead to FDA approval of the underlying product candidate.

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

While we have submitted a CTA module and plan to submit INDs, CTAs or comparable documents for our Rejuva gene therapy candidates, we may not be able to submit such INDs or comparable documents on the timeline we expect. Moreover, we cannot be sure that submission of an IND or CTA or comparable application will result in the FDA or other comparable foreign regulatory authorities allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate clinical studies. These considerations also apply to clinical studies we may submit as amendments to existing INDs or to a new IND. Any failure to submit INDs, CTAs or other comparable documents, on the timelines we expect or to obtain regulatory allowances or other authorizations for any proposed studies may prevent us from completing such clinical studies or commercializing our product candidates on a timely basis, if at all.

Delays or disruptions in regulatory, permit or governmental approval processes may impact our business.

If federal government funding lapses, and/or if federal agencies are unable to perform their usual duties, such as reviewing regulatory submissions, issuing permits, or performing inspections, our business could be adversely affected. For example, a prolonged federal government shutdown could result in delays in regulatory approvals.

Interim, topline and preliminary data from our clinical studies that we announce or publish from time to time may change as more participant 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 participant enrollment continues and more participant 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, serious adverse events 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, adverse events 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 participant recruitment or the ability of enrolled participants 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 participant 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 (“REMS”) or similar mitigation plans in the case of our Rejuva gene therapy candidates, which could include a medication guide outlining the risks of such side effects for distribution to participants;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to participants; 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 participants 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 candidates 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 participants 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 planned Rejuva gene therapy candidates, 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.

The FDA granted Breakthrough Device designation for the Revita DMR System, as an adjunct to diet and exercise, to perform hydrothermal ablation of the duodenal mucosa (the "Revita DMR procedure") for use in the maintenance of weight loss after discontinuation of GLP-1-based therapy on participants who cannot tolerate long-term GLP-1 therapy and who are not candidates for endoscopic remodeling procedure or bariatric surgery. 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.

However, we may not experience a faster development process or review, compared to more conventional procedures and Breakthrough Device designation has no bearing on whether or not the FDA will approve Revita for any indication. 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 U.S., 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 participants 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 (“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 U.S. participate in group purchasing organizations (“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 U.S. 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 candidates because we expect them to be regulated as a combination product.

We expect our Rejuva gene therapy candidates 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 candidates, we may experience delays in the development, approval or certification, and commercialization of our Rejuva gene therapy candidates due to regulatory timing constraints and uncertainties in the product development and approval or certification process. Moreover, although we anticipate that the device component of any combination product candidates we develop will be reviewed within the usual time frames expected for the underlying biologic component application, and that no separate marketing application for the device components of such product candidates will be required in the U.S., the FDA

or comparable regulatory authorities may delay approval or require us to conduct additional studies with respect to any device component, which may delay the approval of the combination product.

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 authorization, 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 U.S., 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 U.S. 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 record keeping 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 (“cGMPs”), or similar foreign requirements, good clinical practice requirements (“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 U.S. 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, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR transition period ended on January 31, 2025, and all clinical trials (and related applications) are now fully subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments.

The EU landscape concerning medical devices recently evolved. On May 25, 2017, the MDR entered into force, which repeals and replaces the MDD and the AIMDD. 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 MDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU and EEA for medical devices and to ensure a high level of safety and health while supporting innovation. See Part I, Item 1, "Business—Government Regulation—Regulation of Medical Devices in the European Union" for more information.

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 candidates 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 (“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 U.S. 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.

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 policy changes, new leadership, 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 (“EMA”), 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, in recent years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities.

If a prolonged government shutdown or similar constraints on funding or staffing occur, or if global health concerns prevent the FDA or other regulatory authorities or notified bodies from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities or notified bodies 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 MDR. Their designation process is significantly stricter under the MDR. Despite a recent increase in designations, the current number of notified bodies designated under the MDR remains significantly lower than the number of notified bodies designated under the previous regime. The current designated notified bodies are therefore facing a backlog of requests as a consequence of which review times have lengthened. This situation could impact our ability to grow our business in the EU and EEA and the ability of the notified body to timely review and process our regulatory submissions and perform its audits.

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 EU, we must comply with the EU medical device vigilance system. Under this system, serious incidents and Field Safety Corrective Actions ("FSCAs") must be reported to the relevant authorities of the EU. 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 ("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 U.S. 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 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 participants, 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.

Our current and potential future use of artificial intelligence technologies may not be successful and presents new risks and challenges to our business.

We currently integrate artificial intelligence (“AI”), technologies in certain areas of our research and development activities, including identification of potential Rejuva product candidates and analysis of preclinical data, and we are seeking to further integrate AI throughout our business. We currently make enterprise third-party AI platforms available to our employees for use in day-to-day business operations and in support of our research and development activities, including tasks such as literature review, data analysis, document drafting, device design optimization, procedural planning and coding for testing/analysis. We are exploring additional opportunities to incorporate AI into our processes for drug discovery, drug development and drug commercialization, and in connection with our enabling functions. In addition, with respect to Revita, we are using AI-driven tools to support manufacturing process improvements, device commercialization and post-market data evaluation. Such efforts may not be successful. Issues relating to the use of new and evolving technologies such as AI may cause us to experience brand or reputational harm, competitive harm, legal liability and new or enhanced governmental or regulatory scrutiny, and we may incur additional costs to resolve such issues.

As with many innovations, AI presents risks and challenges that could undermine or slow its adoption and therefore harm our business. Our use of third-party AI platforms, and any future efforts to develop, test, or deploy additional AI systems, may increase our operating costs due to the nature of the computing costs involved in such systems, which could adversely affect our business, financial condition and results of operation. The use of AI by us and our business partners may lead to novel and urgent cybersecurity risks, which could have a material adverse effect on our operations and reputation as well as the operations of any of our business partners. We may also face increased competition from other companies that are using AI, some of whom may develop more effective methods than we and any of our business partners have, which could have a material adverse effect on our business, results of operations, or financial condition. In addition, our efforts to develop, acquire or integrate these technologies will involve significant time, costs, and other resources, and may divert our management team’s attention and focus from executing on other elements of our strategy. Furthermore, uncertainties regarding developing legal and regulatory requirements and standards may require significant resources to modify and maintain business practices to comply with U.S. and foreign laws concerning the use of AI, the nature of which cannot be determined at this time.

Risks Related to Our Business and Strategy

We are substantially dependent on the success of our lead product candidate, Revita, and our lead gene therapy product candidate, RJVA-001, in the Rejuva platform. 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 and RJVA-001. In 2016, Revita was CE marked under the MDD. The certificate was renewed under the MDD on March 8, 2021. We are investing significant efforts and financial resources in the research and development of Revita, as well as our Rejuva gene therapy candidates including RJVA-001. As part of our Strategic Reprioritization, we intend to prioritize our REMAIN-1 pivotal study, advance Rejuva, and have paused investment in our Revita programs for T2D, including the REVITALIZE-1 study and the Germany Real-World Registry study. 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 in the U.S. We are not permitted to market or promote Revita or any other product candidate, before we receive marketing authorization, approval or certification from the FDA or comparable foreign regulatory authorities or notified bodies, and we may never receive such marketing authorizations, approvals or certifications.

The success of Revita and RJVA-001 will depend on several factors, including the following:

- the successful and timely completion of our ongoing or planned clinical studies;
- the initiation and successful participant 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 U.S. 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 authorization, approval or certification;
- the timely receipt of marketing authorizations, 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 authorizations, approval or certification;
- a continued acceptable safety profile following any marketing authorization or approval;
- commercial acceptance by participants, 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 authorizations, approvals or certification under the MDR 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 participants 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 any future public health crises, including epidemics and pandemics.

In addition, our strategy includes identifying, developing and commercializing our Rejuva gene therapy candidates 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 participants 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 U.S. 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 candidates 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 participants 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 candidates' 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 candidates 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 candidates 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 candidates are 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 candidates 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 candidates, 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 candidates. 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 candidates sufficiently novel or worthy of publication.

We have not yet studied the ability of Revita to be used in repeated procedures. 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 clinical utility and commercial adoption of the device.

We have not yet studied the ability of Revita to be used in repeat procedures. 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 participants who underwent the Revita DMR procedure, in combination with at least one ongoing OAD and lifestyle counseling, we cannot be certain that participants will be able to have repeat procedures in the future. If we are unable to demonstrate the safety of Revita for repeat use, it could have a material adverse effect on the clinical utility and commercial adoption of Revita because providers, referring physicians, payors and participants may not find the product to be a compelling treatment option for people living with obesity or T2D. To the extent any of the aforementioned groups do not accept Revita as a compelling treatment option for people living with obesity or T2D, it could significantly harm our business, financial condition and prospects.

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

We have never obtained marketing authorization for a product candidate in the U.S. It is possible that the FDA may refuse to accept for substantive review any De Novo classification requests, 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 authorization. We believe our proposed approach of treating people living with obesity or T2D through the Revita DMR procedure and our Rejuva gene therapy candidates is novel and, as a result, the process for, and the outcome of, our efforts to seek FDA marketing authorization is especially uncertain.

If the FDA does not accept or grant our De Novo classification request for Revita, or does not accept or approve any BLAs we may submit for our other product candidates, the FDA may require that we conduct additional clinical, preclinical, or manufacturing validation studies and submit that data before it will reconsider our applications. Additionally, if unforeseen safety events arising from the REMAIN-1 study or other ongoing clinical activities cause the FDA to reassess Revita's classification and determine that Revita should be reclassified as a Class III device, we may be required to pursue PMA approval rather than De Novo classification, which would significantly increase the data requirements, time, and cost necessary to obtain marketing authorization. Depending on the extent of these or any other FDA-required studies or a change in required pathway, authorization of any application 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 grant our De Novo classification request, approve our BLAs, or support any required PMA application.

Any delay in obtaining, or an inability to obtain, marketing authorization 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 participants 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 candidates, 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 Revita, our Rejuva gene therapy candidates and any of our other future product candidates in the U.S. 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 participants, that the Revita DMR procedure and our Rejuva gene therapy candidates are superior and attractive alternatives to currently available treatment options. Acceptance of our Rejuva gene therapy candidates and the Revita DMR procedure depends on establishing their safety and effectiveness, including the Revita DMR procedure's durability in treating obesity or 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 participants may elect not to undergo the Revita DMR procedure or take our Rejuva gene therapy candidates.

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 participants 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 candidates are an appropriate option for treating metabolic diseases, such as obesity and 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 participants 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 candidates 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 participants 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 plan to execute an efficient “hub-and spoke” commercialization strategy to position Revita as a novel procedural therapy to treat obesity and T2D and drive its rapid adoption. Leveraging key learning and insights from our Revita clinical program, we plan to have a targeted sales force initially focusing on centers of excellence with metabolically focused GI endoscopists and surgical endoscopists with a dedicated interest in bariatric and metabolic endoscopy. 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 a focus on patients directly within GI endoscopy suites and practices, as well as direct marketing campaigns to raise awareness amongst patients for a compelling new treatment alternative in weight maintenance and obesity. However, the initial point of contact for many patients suffering from obesity and/or T2D may be primary care physicians (“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, obesity and/or 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 candidates 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 candidates, or do not modify their current referral pattern to refer obesity and/or T2D patients to GI endoscopists and surgical 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 candidates. 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, obesity and diabetes management and biopharmaceutical markets are highly competitive. We face significant competition, including companies developing endoscopic, duodenum-targeted metabolic interventions that may compete with our product candidates, 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 obesity specialists, 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 obesity specialists, 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 candidates;
- 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 candidates, 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 U.S. 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 participants 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, via advances in existing technological approaches or the development of new or different approaches, such as using AI and machine learning, 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 obesity specialists, diabetologists, gastroenterologists, interventional endoscopists, endocrinologists, PCPs or other referring physicians, or participants, 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 obesity specialists, 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.

The medical community and third-party payors may choose not to use or 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 obesity specialists, diabetologists, gastroenterologists and interventional endoscopists in treating patients with obesity, T2D and other metabolic diseases. The safety and effectiveness of the Revita DMR procedure and our Rejuva gene therapy candidates 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 candidates, obesity specialists, 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 candidates. 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 candidates, 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, both internal and those provided by third-party providers, 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.

Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our Rejuva gene therapy candidates, 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 candidates.

Our Rejuva gene therapy candidates involve 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 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 or notified bodies, 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 and supply 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, for the device component of the Rejuva product 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 currently manage the final assembly and testing of Revita at our headquarters located in Burlington, Massachusetts, except for the sterilization of the Revita DMR single-use disposable components, including the Revita DMR catheter, and the device component of the Rejuva product, which are 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 any future public health crises, including epidemics and pandemics, impact 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 disease and the actions undertaken to contain the disease or treat its effects.

Additionally, trade policies and geopolitical disputes and other international conflicts can result in tariffs, sanctions and other measures that restrict international trade, and can materially adversely affect our business, particularly if these measures affect regions where manufacturing and product development activities take place or raw materials are sourced. See “Risks Related to Our Financial Condition and Capital Requirements—Unfavorable global economic conditions, including any adverse macroeconomic conditions or geopolitical events, including the conflict between Ukraine and Russia, the conflict between Israel and Hamas, the conflict between Iran and U.S. and recent bank failures affecting the financial services industry, have affected and could further adversely affect our business, financial condition, results of operations or liquidity, either directly or through adverse impacts on certain of the third parties on which we rely to conduct certain aspects of our preclinical studies or clinical studies.”

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;
- the misappropriation of our proprietary information, including our trade secrets and know-how; and
- geopolitical or macroeconomic factors.

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 planned contract manufacturing partners for the production of sub-assembly components of Revita, such as the Revita DMR catheter, Revita console and Rejuva catheter. We rely on a third party manufacturer to manufacture and supply cGMP-grade RJVA-001 for our first-in-human clinical trials. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the U.S. 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 the use of their manufacturing facilities in connection with our product candidates. 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.

Certain Chinese biotechnology companies, CROs and contract development and manufacturing organizations may become subject to trade restrictions, sanctions, other regulatory requirements, or proposed legislation by the U.S. government, which could potentially impact services available for our research and development or our ability to secure the materials we need for our drug candidates. For example, on December 18, 2025, President Trump signed the National Defense Authorization Act for Fiscal Year 2026 into law, which includes the BIOSECURE Act. The BIOSECURE Act prohibits the U.S. government from procuring or obtaining biotechnology equipment or services produced or provided by a “biotechnology company of concern” (“BCC”); entering into, extending, or renewing government contracts with an entity that directly or indirectly uses biotechnology equipment or services from a BCC in performance of that federal contract; and/or issuing grants or loans to purchase, obtain, or use biotechnology equipment or services produced by a BCC. The BIOSECURE Act also prohibits U.S. government loan and grant recipients from using federal loan or grant money to enter into contracts with entities that use equipment from BCCs in the performance of any federal prime contract or subcontract. Companies designated as a BCC include those that are identified on the U.S. Department of Defense’s annual List of Chinese Military Companies, also known as the 1260H List. The U.S. government also has the ability to designate entities as BCCs through a separate designation process. There is a “safe harbor” provision providing that the restrictions do not apply to equipment or services that were formerly but are no longer provided by a BCC, as well as a “grandfathering” provision providing that the prohibitions shall not apply for a five-year period to biotechnology equipment or services produced or provided under a contract or agreement entered into before the applicable effective date. It is unclear whether the grandfathering provision would apply to entities designated as BCCs due to their inclusion on the 1260H List. The guidance to be issued by the Office of Management and Budget regarding implementation of the BIOSECURE Act may provide further clarity on this point. Given the BIOSECURE Act, we may be restricted in our ability to work with certain Chinese biotechnology companies to the extent we would contract with, or otherwise receive funding from, the U.S. government. We do business with companies in China, and it is possible that some of our contractual counterparties could be impacted by the BIOSECURE Act. In addition, such counterparties may be subject to additional U.S. legislation, sanctions, trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. Such disruption could have adverse effects on the development of our drug candidates.

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 authorization or 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 currently known as the Quality Management System Regulation (“QMSR”). The QMSR 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 QMSR 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 authorization of a De Novo application, or 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 U.S., our products and operations are also often required to comply with standards set by industrial standards bodies, such as the International Organization for Standardization. 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 or notified bodies, 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 candidates' 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 candidates' manufacturing process, shortages of raw materials or failure of our suppliers of plasmids and viruses to manufacture and deliver necessary components could result in delays in our Rejuva gene therapy candidates' 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 candidates 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 candidates will be tested for contamination prior to release, if a contaminated product was administered to a participant in any future clinical studies, it could result in harm to the participant. 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 candidates 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 Burlington, 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 REMAIN-1 pivotal clinical study of Revita, and potential future clinical study of RJVA-001. 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 participants 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 ten 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 (“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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information and their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions;
- 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), certain non-physician providers (such as physician assistants and nurse practitioners), and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician’s immediate family members;
- 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 certain regulatory licenses to manufacture or distribute our products commercially and/or the registration of medical device and/or pharmaceutical sales representatives; and state and local laws that require 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 pricing, gifts, compensation and other remuneration provided to physicians and other health care providers or marketing expenditures.

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 purchasers 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 and pharmaceutical 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 U.S. healthcare system. Outside of the U.S., 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 (the "ACA"), made a number of substantial changes in the way healthcare is financed by both governmental and private insurers, including: establishing 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; implementing 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 expanding the eligibility criteria for Medicaid programs.

Certain provisions of the ACA have been subject to judicial and Congressional challenges. For example, on July 4, 2025, the One Big Beautiful Bill Act (the "OBBBA"), was signed into law, which narrowed access to ACA marketplace exchange enrollment and declined to extend the ACA enhanced advanced premium tax credits that expired at the end of 2025, which, among other provisions in the law, are anticipated to reduce the number of Americans with health insurance. The OBBBA also is expected to reduce Medicaid spending and enrollment by implementing work requirements for some beneficiaries, capping state-directed payments, reducing federal funding, and limiting provider taxes used to fund the program. Congress is considering proposed legislation intended to further reduce healthcare costs with alternatives to replace the expired ACA subsidies. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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 2032, 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 (“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.

The current administration is pursuing policies to reduce regulations and expenditures across government agencies including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. For example, the current administration has announced agreements with pharmaceutical companies that require the drug manufacturers to offer, through a direct-to-consumer platform (“TrumpRx”), U.S. patients and Medicaid programs prescription drug Most-Favored Nation pricing equal to or lower than those paid in other developed nations, with additional mandates for direct-to-patient discounts and repatriation of foreign revenues. Other recent actions, for example, include (1) directing agencies to reduce agency workforce and cut programs; (2) directing HHS and other agencies to lower prescription drug costs through a variety of initiatives; (3) imposing tariffs on imported pharmaceutical products; and (4) as part of the Make America Healthy Again Commission’s Strategy Report released in September 2025, working across government agencies to increase enforcement on direct-to-consumer pharmaceutical advertising. Additionally, the current administration recently called on Congress to enact “The Great Healthcare Plan,” to codify and expand Most-Favored Nation pricing, lower government subsidies to private insurance companies, increase healthcare price transparency, expand pharmaceutical drugs available for over-the-counter purchase, and enact restrictions on pharmacy benefit manager payment methodologies, among other things. These actions and policies may significantly reduce U.S. drug prices, potentially impacting manufacturers’ global pricing strategies and profitability, while increasing their operational costs and compliance risks. In June 2024, in *Loper Bright Enterprises v. Raimondo*, the U.S. Supreme Court greatly reduced judicial deference to regulatory agencies, which could increase successful legal challenges to federal regulations affecting our operations. Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program.

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.

In the EU, similar developments may affect our ability to profitably commercialize our product candidates, if approved or certified. On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment (“HTA”), amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product, i.e. oncology and advanced therapy medicinal products as of 2025, certain high-risk medical devices as of 2026, orphan medicinal products as of 2028, and all other medicinal products by 2030. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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. For example, HHS imposes rebates on many Medicare Part B and Medicare Part D products to penalize price increases that outpace inflation on an annual basis. HHS has also been empowered to negotiate the price of certain single-source biologics that have been on the market for at least eleven (11) years covered under Medicare as part of the Medicare Drug Price Negotiation Program. Each year up to twenty (20) products will be selected by HHS for the Medicare Drug Price Negotiation Program. Products subject to the Medicare Drug Price Negotiation Program are expected to experience a significant reduction in reimbursement from the Medicare program on a per unit basis. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our current and any future product candidates that we develop, which could have an adverse effect on our operating results and our overall financial condition. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products or procedures using these products. In the U.S., 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 U.S., 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 numerous data privacy and security obligations, such as various federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that govern data privacy and security), guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to 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 U.S., 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.

Numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018 (“CCPA”) applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA provides for fines and allows private litigants affected by certain data breaches to recover significant statutory damages. The CCPA and other comprehensive U.S. state privacy laws exempt some data processed in the context of clinical trials, but these developments may further complicate compliance efforts and increase legal risk and compliance costs for us and the third parties with whom we work. Similar laws are being considered in several other U.S. states, as well as at the federal and local levels, and we expect more U.S. states to pass similar laws in the future.

We are subject to rapidly evolving data protection laws, rules and regulations in foreign jurisdictions. For example, the European Union General Data Protection Regulation (“EU GDPR”) governs certain collection and other processing activities involving personal data about individuals in the European Economic Area (“EEA”), and the UK General Data Protection Regulation and UK Data Protection Act 2018 (“UK GDPR”), governs similar collection and other processing activities involving personal data about individuals in the United Kingdom. Among other things, the GDPR imposes requirements regarding processing data relating to an identifiable living individual or “personal data,” including health and other sensitive data, including a principle of accountability and the obligation to demonstrate compliance through policies, procedures, training and audit, as well as regulating cross-border transfers of personal data out of the EEA and the UK. The GDPR imposes substantial fines for breaches and violations, which can be up to 20 million Euros under the EU GDPR, 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. Similarly, Australia’s Privacy Act 1988 (*Cth*) (the “Privacy Act”) and the Australian Privacy Principles contained in the Privacy Act impose requirements for transparency, security and data subject rights and provides for penalties of greater of (i) AUD\$ 50 million, (ii) three times the benefit of a contravention, or (iii) 30% of domestic turnover.

In the ordinary course of business, we transfer personal data from Europe and other jurisdictions to the U.S. or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal

data to other countries. In particular, the EEA and the UK have significantly restricted the transfer of personal data to the U.S. and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt or have already adopted similarly stringent data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the U.S. in compliance with law, such as the EU's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto ("DPF") (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the DPF), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the U.S. As the regulatory guidance and enforcement landscape in relation to data transfers continue to develop, we could suffer additional costs, complaints and/or regulatory investigations, fines, or injunctions against our processing or transferring of personal data necessary to operate our business. We may have to stop using certain tools and vendors and make other operational changes, implement alternative data transfer mechanisms under the GDPR and/ or take additional compliance and operational measures.

Additionally, the U.S. Department of Justice issued a rule entitled the Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons, which places additional restriction on certain data transactions involving countries of concern (e.g., China, Russia, Iran) and covered persons (i.e., individuals and entities who are designated as such by the U.S. Attorney General or considered "foreign persons" and are majority owned by, organized under the laws of, a primary resident in, or a contractor of, a covered person or country of concern, as applicable) that may impact certain business activities such as vendor engagements, sale or sharing of data, employment of certain individuals, and investor agreements. Violations of the rule could lead to significant civil and criminal fines and penalties. The rule applies regardless of whether data is anonymized, key-coded, pseudonymized, de-identified or encrypted, which presents particular challenges for companies like ours and may impact our ability to engage in transactions or agreements with certain third parties in the future.

We are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the GDPR and the CCPA, require our customers to impose specific contractual restrictions on their service providers. We publish privacy policies, marketing materials, and other statements, such as statements concerning data privacy, and security. We also include privacy statements in our informed consent forms for study subjects and have associated privacy notices available if requested.

Regulators in the U.S. are increasingly scrutinizing these statements, and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

In addition, we use artificial intelligence, machine learning, and automated decision-making technologies (collectively, "AI Technologies") in our business. Our employees and personnel use generative artificial intelligence ("AI") and automated decision-making technologies to perform their work, and the disclosure and use of personal data in AI technologies is subject to various privacy laws and other privacy obligations. The regulatory framework for AI Technologies is rapidly evolving as many federal, state, and foreign government bodies and agencies have introduced or are currently considering additional laws and regulations. Additionally, existing laws and regulations may be interpreted in ways that would affect the operation of AI Technologies. As a result, implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or market perception of their requirements may have on our business and may not always be able to anticipate how to respond to these laws or regulations.

It is possible that new laws and regulations will be adopted in the U.S. and in other non-U.S. jurisdictions, or that existing laws and regulations, including competition and antitrust laws, may be interpreted in ways that would limit our ability to use AI Technologies for our business, or require us to change the way we use AI Technologies in a manner that negatively affects the performance of our products, services, and business and the way in which we use AI Technologies. We may need to expend resources to adjust our products or services in certain jurisdictions if the laws, regulations, or decisions are not consistent across jurisdictions. Further, the cost to comply with such laws, regulations, or decisions and/or guidance interpreting existing laws, could be significant and would increase our operating expenses (such as by imposing additional reporting obligations regarding our use of AI Technologies). Such an increase in operating expenses, as well as any actual or perceived failure to comply with such laws and regulations, could adversely affect our business, financial condition and results of operations.

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.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties with whom we work may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties with whom we work fail, or are perceived to have failed, 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 (including class-action claims) and mass arbitration demands, additional reporting requirements and/or oversight, bans or restrictions on processing personal data, orders to destroy or not use personal data, and imprisonment of company officials. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: interruptions or stoppages in our business operations (including, as relevant, clinical trials), inability to process personal data or to operate in certain jurisdictions, limited ability to develop or commercialize our products, expenditure of time and resources to defend any claim or inquiry; adverse publicity, or substantial changes to our business model or operations.

We are subject to U.S. and certain foreign anti-corruption laws and regulations, export and import controls, sanctions and embargoes. We could face liability and other serious consequences for violations which can harm our business.

We are subject to anti-corruption laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "FCPA"), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act and other state and national anti-bribery laws in the countries in which we may conduct activities in the future. Anti-corruption laws are interpreted broadly and generally prohibit companies and their employees, agents, contractors and other third-party collaborators from offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly through third parties, to any person in the public or private sector to obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

We are also subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Compliance with applicable regulatory requirements regarding the export of our product candidates and technology may create delays in the introduction of our product candidates and technology in international markets or, in some cases, prevent the export of our product candidates and technology to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments and persons targeted by U.S. sanctions.

There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors or collaborators, or those of our affiliates, will comply with all applicable anti-corruption, export and import control, and sanctions laws and regulations. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our product candidates and technology in one or more countries as well as difficulties in manufacturing or continuing to develop our product candidates, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results and financial condition.

We are subject to complex and changing laws and regulations, which exposes us to potential liabilities, increased costs and other adverse effects on our business.

We are subject to complex and changing laws, regulations, and executive orders, and compliance with these laws and regulations and executive orders, as well as changing interpretations, policies, and enforcement priorities related to such laws, regulations, and executive orders, is onerous and expensive. Compliance with such laws, regulations, and executive orders can adversely affect our business by increasing our costs, limiting our ability to pursue or offer a product candidate or product, and requiring changes to our business. New and changing laws, regulations, and executive orders can also create uncertainty about how such laws and regulations will be interpreted, prioritized, or applied. Regulatory changes and other actions that materially adversely affect our business may be announced with little or no advance notice we may not be able to effectively mitigate all adverse impacts from such measures. Differing interpretations of such legal obligations and policy changes or changes in enforcement priorities can expose us to significant fines, government investigations, litigation and reputational harm. If we are found to have violated laws, regulations, or executive orders, it could materially adversely affect our business, reputation, results of operations and financial condition.

Damage to our reputation or brand image could adversely affect our sales and results of operations.

Incidents that erode trust or confidence in us could adversely affect our reputation and thereby impact our business, particularly if the incidents result in rapid or significant adverse publicity, protests, litigation, boycotts, governmental inquiries, or other stakeholder responses. This could include incidents regarding our actions or inactions on issues related to corporate social responsibility or environmental, social, and governance (“ESG”) matters. Any goals and initiatives that we establish on ESG matters, including with respect to sustainability and diversity, equity, and inclusion topics, are subject to risk. We cannot guarantee that we will achieve and goals and initiatives that may from time to time set. Any failure, or perceived failure, by us to achieve such goals and initiatives could adversely affect our reputation. Further, stakeholder expectations regarding ESG matters continue to evolve and are not uniform, and our pursuit of our goals and initiatives could adversely impact our reputation due to such differing expectations and opinions regarding such goals and initiatives. In turn, damage to our reputation or brand image could, among other things, adversely impact our relationships with third parties, our business opportunities, our ability to attract and retain talent sufficient to meet business needs, and results of operations. Any of the foregoing can be further exacerbated by changes to laws, regulation, standards and executive orders. See “—We are subject to complex and changing laws and regulations, which exposes us to potential liabilities, increased costs and other adverse effects on our business.”

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 U.S. 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 U.S. Patent and Trademark Office (“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 U.S., and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions.

Because patent applications in the U.S., 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 U.S., 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 (“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 U.S., 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 U.S. 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 U.S., and the laws of some foreign countries do not provide patent protection for certain types of inventions that are patentable in the U.S. 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 U.S., including in Europe, and our intellectual property rights outside the U.S. could be less extensive than those in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. 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.

Moreover, geo-political actions in the U.S. and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the U.S. and foreign government actions related to Russia's conflict with Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. For example, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the U.S. without consent or compensation. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S. or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the U.S. These products may compete with our product candidates and our patents or other IP rights may not be effective or sufficient to prevent them from competing.

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 U.S. 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 U.S. 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. 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. There may be patents 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 U.S., 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 us 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 U.S. 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.

On June 1, 2023, the European Union Patent Package (“EU Patent Package”), regulations were implemented with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court (“UPC”), for litigation involving European patents. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC, unless otherwise opted out. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. During the first seven years of the UPC’s existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. We decided to opt out our European patents from the UPC, and doing so may preclude us from realizing the benefits of the UPC.

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 U.S. 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 U.S. 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 U.S., 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 U.S. 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. We may also need to share our proprietary information, including trade secrets, with our current and future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. The failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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 U.S.;
- 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 have a small market development team. In order to commercialize any product candidates, if approved, we must build marketing, sales, reimbursement and market access, 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 authorization, 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 authorization, 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 President and Chief Product Officer, and Lara Smith Weber, our Chief Financial Officer and Treasurer, 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, including as we realign our business in accordance with the Strategic Reprioritization, 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.

As part of the Strategic Reprioritization, we announced that we streamlined resources, including a workforce reduction impacting 22 employees. In light of this workforce reduction, we may find it difficult to maintain valuable aspects of our culture, to prevent a negative effect on employee morale or attrition beyond our planned workforce reduction, and to attract competent personnel who are willing to embrace our culture in the future.

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, recruit, integrate, motivate 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, including our Strategic Reprioritization we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of March 1, 2026, we have 100 full-time employees, including 73 employees engaged in research and development. In order to successfully implement our development and commercialization plans and strategies, and as we are 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, retaining 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 authorization or 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 Ownership of Our Common Stock

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 may 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.

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 Part I, Item 1A. Risk Factors and elsewhere in this Annual Report on Form 10-K, 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 U.S. 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 impact of any future public health crises, including epidemics and pandemics, and actions taken to slow their spread; and
- general economic, geopolitical, 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 Part I, Item 1A. Risk Factors, could have a dramatic and adverse impact on the market price of our common stock.

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 is influenced by the research and reports that securities or industry analysts publish about us, our business or our market. 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.

As of March 1, 2026, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 29% of our voting stock, including securities currently exercisable or convertible into voting stock. Therefore, these stockholders are able to influence us through this ownership position. These stockholders may be able to impact all matters requiring stockholder approval. For example, these stockholders may be able to impact 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.

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 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.

As of March 1, 2026, we had outstanding a total of 158,648,963 shares of our common stock. All shares of our common stock that were sold in our IPO are freely tradable without restriction or further registration under the Securities Act of 1933, as amended (“Securities Act”), unless held by our “affiliates” as defined in Rule 144 under the Securities Act. Subject to applicable securities law restrictions, the shares previously subject to lock-up agreements in connection with our IPO are now able to be sold in the public market. We have filed a registration statement on Form S-8 under the Securities

Act to register shares issued upon the exercise of stock options, RSUs and warrants outstanding under our equity incentive plans or pursuant to future awards granted under those plans. Accordingly, shares registered under the registration statement on Form S-8 will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, and subject, in the case of affiliates, to volume, manner of sale and other limitations under Rule 144.

Upon the completion of our IPO in February 2024, the holders of approximately 38,518,563 shares of our common stock have rights, subject to some conditions, to require us to file registration statements covering the sale of their shares (including additional shares of our common acquired by such holders after the IPO, subject to the terms of our fifth amended and restated investors' rights agreement) or to include such shares in registration statements that we may file for ourselves or our other stockholders. Once we register the offer and sale of shares for the holders of registration rights, these shares will be able to be sold in the public market without volume or manner of sale limitations.

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. Furthermore, we are a party to a credit agreement that contains negative covenants that limit our ability to pay dividends. For more information, see Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources."

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 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 so that not all members of our board of directors (the "Board") are elected at one time;
- permit only the Board 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 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 (“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 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 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 also provide that the federal district courts of the U.S. 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 information technology systems, or those of any of our CROs, manufacturers, third-party service providers, 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 information technology 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. Our information technology systems, while appropriate for our current operations, are potentially vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees or vendors, or from attacks by malicious third parties. Such attacks are prevalent and increasing in their frequency, levels of persistence, levels of sophistication and intensity, are increasingly difficult to detect, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise including traditional computer “hackers,” threat actors, “hacktivists,” organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors, especially given increased vulnerability of corporate information technology systems as distributed work environments have become prevalent.

In addition to unauthorized access to or acquisition of personal data, confidential information, intellectual property or other sensitive information, such attacks could include the deployment of harmful malware and ransomware, and may use a variety of methods, including denial-of-service attacks, social engineering (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), credential stuffing attacks, credential harvesting, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, and other similar threats, to attain such unauthorized access or acquisition or otherwise affect service reliability and threaten the confidentiality, integrity and availability of information. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, ability to provide our products or services, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments.

Like many other companies, we experience attempted cybersecurity actions on a frequent basis, and the frequency of such attempts could increase in the future. While we have invested in the protection of data and information technology, there can be no assurance that our efforts will prevent, quickly identify, mitigate, contain, or remediate service interruptions or security breaches. We cannot assure that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages or breaches in our systems or those of our third-party services providers or partners. Actions taken by us or the third parties with whom we work to detect, investigate, mitigate, contain, and remediate a security incident could result in outages, data losses, and disruptions of our business.

We take steps designed to detect, mitigate, and remediate vulnerabilities in our information systems (such as our hardware and/or software, including that of third parties with whom we work). We have not and may not in the future, however, detect and remediate all such vulnerabilities including on a timely basis. Further, we have and may in the future experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

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, or give the perception of interruptions or unauthorized acquisitions, 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. 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 (including class claims) and governmental enforcement actions (for example, investigations, fines, penalties, audits, and inspections), indemnification obligations, negative publicity, reputational harm, monetary fund diversions, diversion of management attention, additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data), financial loss, and other similar harms.

Any of the previously identified or similar threats have in the past and may in the future cause a security incident or other interruption that have in the past and may in the future result in unauthorized, unlawful, or accidental acquisition,

modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties with whom we work. A security incident or other interruption could disrupt our ability (and that of third parties with whom we work) to conduct clinical trials. We may expend significant resources or modify our business activities including our clinical trial activities to try to protect against security incidents. Certain data privacy and security obligations have required us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and sensitive information.

Some of the federal, state and foreign government requirements include obligations of companies to notify relevant parties including affected individuals and regulators 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. We may also voluntarily choose to notify said stakeholders. 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. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If the third parties with whom we work experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if the third parties with whom we work fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or that of the third parties with whom we work have not been compromised.

Our contracts may not contain relevant limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. 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 (including those caused or exacerbated by climate change) 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:

- 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 Annual Report on Form 10-K and our other 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 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 \$1.235 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 IPO.

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 being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Part II, Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations disclosure in this Annual Report on Form 10-K and scaled 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 (“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 are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection 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 Annual Report on Form 10-K 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 are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are a low revenue 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 U.S. 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 U.S. tax laws and regulations or the interpretation of them;
- 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;
- limitations or adverse findings regarding our ability to do business in some jurisdictions; and

- On July 4, 2025, the OBBB Act, which includes a broad range of tax reform provisions, was signed into law in the U.S. and we continue to assess its impact.

If our product candidates are authorized or 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 authorizations or 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, including tariffs;
- 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.

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 Inflation Reduction Act, among other changes, introduced a 15% corporate minimum tax on certain U.S. corporations and a 1% excise tax on certain stock redemptions by U.S. corporations. On July 4, 2025, the OBBB Act, which includes a broad range of tax reform provisions, was signed into law in the U.S. and we continue to assess its impact. We currently do not expect the OBBB Act to have a material impact on our estimated annual effective tax rate in 2025. We are unable to predict which, if any, additional U.S. tax reform proposals will be enacted into law, and what effects the OBBB Act or any other enacted legislation might have on our tax liabilities.

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.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity, and availability of our critical systems and information.

We designed and assessed our program based on the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF). This does not imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program is integrated into our overall risk management program, and shares common methodologies, reporting channels and governance processes that apply across the risk management program to other legal, compliance, strategic, operational, and financial risk areas.

Key elements of our cybersecurity risk management program include but are not limited to the following:

- risk assessments designed to help identify material risks from cybersecurity threats to our critical systems and information;
- a security team principally responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls, and (3) our response to cybersecurity incidents;
- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security processes;
- cybersecurity awareness training of our employees, including incident response personnel, and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- a third-party risk management process for key service providers, based on our assessment of their criticality to our operations and respective risk profile.

We face risks from cybersecurity threats that, if realized, are reasonably likely to materially affect us, including our operations, business strategy, results of operations, or financial condition. See Part I, Item 1A, “Risk Factors—General Risks—Our information technology systems, or those of any of our CROs, manufacturers, third-party service providers, 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.”

Cybersecurity Governance

Our Board considers cybersecurity risk as part of its risk oversight function and has delegated to the audit committee oversight of cybersecurity risks including oversight of management’s implementation of our cybersecurity risk management program. Pursuant to its charter, the audit committee’s oversight of the integrity of our information technology systems and cybersecurity risks includes the review and assessment with management of the adequacy of controls and security for our information technology systems, processes and data, as well as our contingency plans in the event of a breakdown or security breach affecting our information technology systems.

As part of its oversight, the audit committee will receive reports from management on our cybersecurity risks including any material cybersecurity incidents, as well as any incidents with lesser impact potential.

The audit committee reports to the full Board regarding its activities, including those related to cybersecurity. In addition, management may from time to time directly provide the full Board with briefings on our cyber risk management program, including presentations on cybersecurity topics from our Security Officer, internal security staff or external experts as part of the Board's continuing education on topics that impact public companies.

The Company engages third party service providers to provide information technology and cybersecurity services, including advising management on information technology strategy, infrastructure, and cybersecurity matters. In addition, the Company employs an Information Technology Manager who supports the day-to-day operation and maintenance of the Company's information technology systems and assists with the implementation and maintenance of cybersecurity controls and procedures in collaboration with the Company's IT and cybersecurity consultants.

Our interim Vice President of Information Technology, who reports to the Chief Executive Officer, is responsible for assessing and managing the Company's material risks from cybersecurity threats and overseeing the Company's cybersecurity risk management program. This includes supervision of internal information security personnel and retained external cybersecurity consultants.

The interim Vice President of Information Technology has more than 20 years of experience in information technology leadership, including responsibility for information security, data privacy, and regulatory compliance across life sciences organizations, including biotechnology and medical device companies. Over the past six years, he has overseen enterprise cybersecurity programs at life sciences companies across both pre-commercial and commercial stages, supporting regulatory, quality, and compliance requirements.

Our management team takes efforts designed to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in the IT environment.

Item 2. Properties.

Our corporate headquarters is located at 3 Van de Graaff Drive, Suite 200, Burlington, Massachusetts, 01803, where we currently lease office and laboratory space of approximately 78,000 square feet under a lease agreement which will expire in June 2034, subject to earlier termination or extension. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed. As of March 1, 2026, 82 of our employees are located at our corporate headquarters.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings. From time to time, we may become party to various lawsuits, claims and other legal proceedings that arise in the ordinary course of business.

Item 4. Mine Safety Disclosures.

Not Applicable.

PART II

Item 5. Market For Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

On February 2, 2024, our common stock began trading on the Nasdaq Global Market under the symbol “GUTS.” Prior to that time, there was no public market for our common stock.

Holder

As of March 1, 2026, we had approximately 50 holders of record of our common shares. This number does not include beneficial owners whose shares were held in street name.

Dividends

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.

Recent Sales of Unregistered Securities

Pre-Funded Warrant Exchange

On November 12, 2025, we entered into an exchange agreement with entities affiliated with Nantahala Capital Management (the “Holders”), pursuant to which the Holders agreed to exchange an aggregate of 4,850,000 shares of common stock for pre-funded warrants (the “Exchange Warrants”) to purchase up to 4,850,000 shares of common stock at an exercise price of \$0.001 per share (the “Exchange”).

The Exchange Warrants are exercisable immediately and may be exercised at any time until all of the Exchange Warrants are exercised in full. A Holder may not exercise any portion of an Exchange Warrant to the extent that, immediately prior to or after giving effect to such exercise, the Holder (together with its affiliates and other attribution parties) would own more than 9.99% of our outstanding common stock immediately after exercise, which percentage may be changed at the Holder’s election to a lower or higher percentage not in excess of 19.99% upon 61 days’ notice to us, subject to the terms of the Exchange Warrants. The Exchange Warrants were issued without registration under the Securities Act, in reliance on the exemption from registration contained in Section 3(a)(9) of the Securities Act.

Subsequent to the Exchange, in January 2026 all Exchange Warrants for 4,850,000 shares of our common stock were exercised at an exercise price of \$0.001 per share.

Purchases of equity securities by the issuer and affiliated purchasers

None.

Item 6. [Reserved].

Item 7. 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 our consolidated financial statements and related notes and other information included elsewhere in this Annual Report on Form 10-K. 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, assumptions, and other important factors. 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 Part I, Item 1A. Risk Factors and the section titled “Forward-Looking Statements” included elsewhere in this Annual Report on Form 10-K. 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 a clinical-stage metabolic therapeutics company focused on pioneering novel approaches to treat obesity and type 2 diabetes (“T2D”). Our Revita[®] and Rejuva[®] candidates are designed to target root causes of metabolic diseases, allowing us to advance metabolic disease treatment from chronic management towards prevention and reversion of the disease. For a detailed description of our business, product candidates, and development programs, see Part I, Item 1, “Business.”

Key Developments During 2025

During the year ended December 31, 2025, we made significant progress advancing our two product candidates:

Revita. We completed enrollment of the REMAIN-1 Pivotal Cohort in July 2025, a randomized, double-blind, sham-controlled pivotal study evaluating the safety and efficacy of Revita in maintaining weight loss after GLP-1 based therapy discontinuation. We completed randomization of the pivotal cohort in February 2026, with topline six-month data anticipated in the early fourth quarter of 2026.

Strategic Reprioritization. On January 31, 2025, we announced our Strategic Reprioritization, announcing we paused investment in our Revita for T2D, including the REVITALIZE-1 study and the Germany Real-World Registry study. Our decision to pause these studies was not driven by any safety or efficacy concerns. We continue to follow existing participants per protocol and report outcomes on an ongoing basis for these studies. The Strategic Reprioritization included a workforce reduction impacting 22 employees, or approximately 17% of our workforce, and has been substantially implemented.

Rejuva. We completed key preclinical *in vivo* studies to support clinical trial applications (“CTAs”) for RJVA-001, our lead gene therapy candidate and subsequently submitted CTAs for RJVA-001 in T2D to regulators in the EU (Netherlands) and Australia in the second half of 2025, advancing the program toward its anticipated first-in-human study. We also advanced RJVA-002, our dual GIP/GLP-1 gene therapy candidate, through preclinical development.

Anticipated 2026 Revita Milestones

With randomization complete, we are advancing toward multiple anticipated clinical and regulatory milestones toward pivotal readout and potential U.S. regulatory submission. In March 2026 in connection with its regulatory strategy, the Company received pre-submission feedback from the FDA in which it acknowledged that the safety profile of the Revita DMR System, based on clinical data from over 300 procedures, is consistent with a Class II device classification. As in all applications, the FDA indicated that final pathway determinations will be made following review of the complete safety dataset which the Company intends to include in its potential De Novo marketing application submission.

- One-year REVEAL-1 Cohort data in the second quarter of 2026.
- One-year REMAIN-1 Midpoint Cohort randomized data in the third quarter of 2026.
- Topline six-month randomized data from the REMAIN-1 Pivotal Cohort in the early fourth quarter of 2026.
- Potential FDA De Novo marketing application submission in post-GLP-1 weight maintenance in the late fourth quarter of 2026.

Anticipated 2026 Rejuva Milestones

- Regulatory feedback on CTAs for RJVA-001 in the second quarter of 2026.
- First-in-human dosing of RJVA-001, subject to CTA authorization, and expected reporting of preliminary data in the second half of 2026.

We are pursuing opportunities to strengthen our balance sheet and fund our path towards potential commercialization, leveraging the achievement of clinical data milestones.

Management believes that our available cash and cash equivalents balance of \$81.5 million as of December 31, 2025, combined with \$4.1 million in subsequent proceeds from Tranche A warrant exercises received in January 2026, will be sufficient to fund our operating expenses and capital expenditure requirements into early 2027. Importantly, we are well funded through multiple key clinical and regulatory milestones in 2026, including the anticipated topline six-month randomized data from the REMAIN-1 Pivotal Cohort, anticipated De Novo marketing application submission in post-GLP-1 weight maintenance, and initial dosing and preliminary data from our RJVA-001 clinical program. For additional information regarding our liquidity, funding requirements and going concern assessment, see “Liquidity and Capital Resources—Funding Requirements and Going Concern” below and Part I, Item 1A, “Risk Factors—Risks Related to Our Financial Condition and Capital Requirements.”

Components of our Consolidated Results of Operations

Revenue and Cost of Goods Sold

To date, we have generated revenue in Germany since the limited pilot commercial launch of Revita in the first quarter of 2023. We have not generated any revenue in the U.S. and do not expect to generate any revenue there unless and until we successfully complete clinical development and obtain marketing approvals for one or more of our product candidates. On January 31, 2025, we approved a Strategic Reprioritization, in which we have paused investment in our Revita programs for T2D, which consists of the REVITALIZE-1 study and the Germany Real World Registry study. As a result, we have not generated any revenue in 2025.

Cost of goods sold primarily consist of material costs, direct labor, and manufacturing overhead costs. We currently manage the final assembly and testing of Revita in the manufacturing space at our headquarters in Burlington, Massachusetts. We contract with third-party manufacturers to produce certain key parts of our single-use devices and consoles.

Operating Expenses

Research and Development Expenses

Research and development expenses primarily consist of personnel-related expenses, including salaries, bonuses, fringe benefits and stock-based compensation expense, for employees engaged in research and development functions. These expenses also include external costs associated with our ongoing clinical studies, including payments to clinical sites and our clinical research organization (“CRO”) and clinical manufacturing costs, as well as fees paid to third party consultants and contractors for engineering, quality assurance and regulatory support. In addition, research and development expenses include costs associated with our preclinical research and Chemistry, Manufacturing, and Controls (“CMC”) activities 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 current assets or as 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 our CRO, 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)	Year Ended December 31,	
	2025	2024
Direct program-specific expenses:		
Revita	\$ 28,892	\$ 25,873
Rejuva	11,685	7,220
Total direct program-specific expenses	40,577	33,093
Indirect expenses	7,965	9,038
Personnel-related expenses (including stock-based compensation)	25,994	28,340
Total research and development expenses	\$ 74,536	\$ 70,471

We expect our research and development expenses to decrease in the near term as a result of the completion of randomization in the REMAIN-1 pivotal study, as spending shifts from enrollment-related activities to patient follow-up and data collection. This decrease may be partially offset by costs associated with initiating the Rejuva first-in-human study.

Selling, General and Administrative Expenses

Selling, general and administrative expenses primarily consist of personnel-related costs, including salaries, bonuses, fringe benefits and stock-based compensation expense, for our personnel and external contractors involved in our executive, finance, legal, and other administrative functions. Selling, 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 expect our selling, general and administrative expenses to stay stable in the near term. If marketing approval or certification for our product candidate is obtained, we anticipate that our selling, general and administrative expenses will increase over time as we expand our commercial and administrative function to support our transition towards commercial readiness and the potential launch, as well as pursue payor coverage and reimbursement for our current and future product candidates.

Other Income (Expenses), Net

Other income (expense), net is primarily comprised of interest income, change in fair value of notes payable, and change in fair value of warrant liabilities.

Interest Income

Interest income is primarily generated from cash interest earned on our cash, cash equivalents, and restricted cash balances.

Change in Fair Value of Notes Payable

In January 2022, we entered into a financing arrangement with certain lenders in which we issued convertible promissory notes (the “2022 Convertible Notes”). Upon the closing of our IPO in February 2024, all outstanding principal plus accrued interest under the 2022 Convertible Notes were converted into our common stock. The 2022 Convertible Notes were marked to market to their fair value as of the time of the conversion before being reclassified to equity.

In September 2023, we entered into a credit agreement with certain lenders that provides for term loans (the “2023 Notes”). We elected the fair value option to account for these notes payable, which are re-measured at the end of each reporting period with changes in fair value recognized as a component of other income (expense), net. We will continue to recognize changes in fair value of the notes payable until they are repaid in cash.

Change in Fair Value of Warrant Liabilities

In January 2014, we issued a fully vested warrant to purchase shares of our Series B convertible preferred stock in connection with a loan and security agreement entered into in January 2014. In connection with our IPO in February 2024,

warrants to purchase our convertible preferred stock converted into warrants to purchase our common stock and related liabilities were reclassified to additional paid-in capital.

In July 2023, we issued fully vested warrants to purchase shares of our common stock in connection with the issuance of the amended and restated 2022 Convertible Notes. In September 2023, we issued fully vested warrants to purchase shares of our common stock or convertible preferred stock in connection with the 2023 Notes. In August 2025, we issued fully vested warrants to purchase shares of our common stock in connection with our August 2025 Offering.

These warrants were classified as liabilities on our consolidated balance sheet and were initially recorded at fair value on the grant date. They are subsequently remeasured to fair value at the end of each reporting period and at exercise with changes in fair value recognized as a component of other income (expense), net. We will continue to recognize changes in fair value of the warrant liabilities until the warrants are exercised or expire.

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 U.S. 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.

While our significant accounting policies are described in more detail in Note 2 – "Significant Accounting Policies" of our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, 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.

Determination of the Fair Value of Notes Payable

We elected the fair value option to account for our 2023 Notes, and remeasure the fair value at each reporting date. The fair value of the 2023 Notes as of December 31, 2025 and 2024 was estimated using a discounted cash flow model by discounting projected future cash flows associated with the 2023 Notes to their present value. The discount rate used in the model is based on observable market yields for similarly rated instruments, adjusted for any specific risks inherent in the 2023 Notes, which is a level 3 fair value measurement and requires judgment to determine at each period end.

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;
- CRO and investigative sites in connection with preclinical and clinical studies; and

- Clinical Manufacturing Organizations (“CMOs”), 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 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 participants 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

The following table summarizes our consolidated results of operations for the years ended December 31, 2025 and 2024:

(in thousands)	Year Ended December 31,		Change	
	2025	2024	Amount	%
Revenue	\$ —	\$ 93	\$ (93)	(100.0%)
Cost of goods sold	—	50	(50)	(100.0%)
Gross profit	—	43	(43)	(100.0%)
Operating expenses:				
Research and development	74,536	70,471	4,065	5.8%
Selling, general and administrative	22,280	23,103	(823)	(3.6%)
Total operating expenses	96,816	93,574	3,242	3.5%
Loss from operations	(96,816)	(93,531)	(3,285)	3.5%
Other income (expense), net	(44,138)	24,837	(68,975)	(277.7%)
Net loss and comprehensive loss	<u>\$ (140,954)</u>	<u>\$ (68,694)</u>	<u>\$ (72,260)</u>	105.2%

Revenue and Cost of Goods Sold

Revenue and cost of goods sold during the year ended December 31, 2024, was related to our pilot commercial launch in Germany. In January 2025, we approved a Strategic Reprioritization in which we paused investment in our Revita program for T2D, which also included the pilot commercial launch in Germany. Therefore, we did not recognize any revenue in 2025.

Research and Development Expenses

Research and development expenses increased by \$4.1 million, or 5.8%, during the year ended December 31, 2025, as compared to the year ended December 31, 2024, primarily due to the advancements made in our Revita and Rejuva programs.

Revita-related expenses increased by \$3.0 million, mainly due to a \$6.1 million increase in clinical related expenses, partially offset by a \$2.0 million decrease in collaborative medical research expenditures and a \$1.1 million decrease in Revita related engineering expenses. Increases in clinical expenses were primarily driven by the positive progress made in our REMAIN-1 study, partially offset by reduced expenses from the REVITALIZE-1 study as a result of our Strategic Reprioritization, which also contributed to the decrease in collaborative medical research expenditures. Revita related engineering expenses decreased as our development efforts gradually shifted to validation and regulatory approval support

activities. Rejuva-related expenses increased by \$4.5 million as we advanced preclinical CMC activities and clinical preparation work in support of the RJVA-001 first-in-human study.

Personnel related expenses decreased by \$2.3 million, which was mainly the result of a \$3.6 million decrease in stock-based compensation expense, partially offset by a \$1.3 million increase in bonuses, severance and associated payroll taxes. Allocated facilities expenses also decreased by \$1.2 million due to the expenses incurred when we moved into our new office and laboratory space in Burlington, MA in the first quarter of 2024.

Selling, General and Administrative Expenses

Selling, general and administrative expenses decreased by \$0.8 million, or 3.6%, during the year ended December 31, 2025 as compared to the year ended December 31, 2024, primarily due to decreased personnel-related expenses of \$2.9 million driven by a \$4.1 million decrease in stock-based compensation expense, partially offset by a \$1.2 million increase in salary, bonus and severance expenses. This personnel-related decrease was partially offset by a \$1.8 million increase in offering costs primarily associated with the issuance of warrants in the August 2025 Offering and a \$0.7 million increase in legal, audit, investor relations and other administrative expenses incurred to support our operation as a public company.

Other Income (Expense), Net

Other expense, net, of \$44.1 million during the year ended December 31, 2025, was primarily attributable to a \$40.9 million loss from the change in fair value of warrant liabilities, a \$4.7 million loss from the change in fair value of notes payable, partially offset by \$1.5 million in net interest income. Other income, net, of \$24.8 million during the year ended December 31, 2024, was primarily attributable to a \$17.9 million gain from the change in fair value of notes payable, a \$2.8 million gain from the change in fair value of warrant liabilities, and \$4.1 million in net interest income.

Changes in fair value of warrant liabilities and changes in fair value of the 2022 Convertible Notes were mainly a result of the fluctuation of the value of the underlying shares of our common stock. Changes in fair value of the 2023 Notes were primarily driven by a combination of interest on the notes payable and the fluctuation of market interest rates. Interest income earned from our cash deposits decreased by \$2.6 million mainly due to lower overall deposit balances and lower interest rate during 2025 as compared to 2024.

Non-GAAP Financial Measures

In addition to our results determined in accordance with U.S. GAAP, we also evaluate our performance using Adjusted EBITDA, a non-GAAP financial measure. We define Adjusted EBITDA as net loss adjusted to exclude (i) interest income, net, (ii) depreciation expense, (iii) stock-based compensation expense, (iv) changes in the fair value of notes payable and (v) changes in the fair value of warrant liabilities.

We present Adjusted EBITDA as supplemental information because management believes it provides additional insight into our operating performance and facilitates comparisons of our results from period to period by excluding items that are non-cash or non-operational in nature and may vary in magnitude. Management uses Adjusted EBITDA in evaluating our operating performance and in planning and forecasting future periods.

Adjusted EBITDA should not be considered in isolation or as a substitute for, or superior to, net loss or any other measure of financial performance prepared in accordance with GAAP. Adjusted EBITDA does not reflect interest income, depreciation, stock-based compensation expense, or changes in the fair value of certain financial instruments, each of which may be significant. In addition, our definition of Adjusted EBITDA may differ from similarly titled measures used by other companies and therefore may not be comparable.

A reconciliation of net loss, the most directly comparable GAAP financial measure, to Adjusted EBITDA is presented below.

(in thousands)	Year Ended December 31,	
	2025	2024
Net loss and comprehensive loss	\$ (140,954)	\$ (68,694)
Interest income, net	(1,540)	(4,146)
Depreciation	1,129	677
EBITDA	(141,365)	(72,163)
Stock-based compensation expense	6,684	14,426
Change in fair value of notes payable	4,724	(2,830)
Change in fair value of warrant liabilities	40,901	(17,908)
Adjusted EBITDA	\$ (89,056)	\$ (78,475)

Liquidity and Capital Resources

We manage our cash and capital structure to maximize shareholder return, maintain 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.

Loan and Security Agreements

2023 Notes

On September 7, 2023, we entered into a credit agreement, as amended from time to time (the “Credit Agreement”), with Symbiotic Capital Opportunities Holding, L.P. and Catalio Structured Opportunities AIV I LP (the “2023 Lenders”) that provided for term loans up to an aggregate principal amount of \$45.0 million (the “2023 Notes”) in two tranches. The first tranche, with a principal amount of \$30.0 million, was drawn on September 7, 2023, resulting in net proceeds of approximately \$28.4 million. The second tranche, with a principal amount of \$15.0 million, would have been extended upon our achievement of certain operating and funding milestones as defined in the Credit Agreement, by July 31, 2024. The Credit Agreement also provides for a third tranche with an uncommitted principal amount of \$20.0 million that may be extended to us, subject to the 2023 Lenders’ prior written consent in their sole discretion. Due to a shift in business strategy to include the weight maintenance study, we decided not to pursue the milestones required to access the second tranche. As a result, the second tranche was not extended.

The Credit Agreement, as amended, contains financial covenants including a minimum liquidity covenant requiring us to maintain a minimum \$10.0 million balance in cash and cash equivalents on deposit in accounts, subject to certain exceptions. As of December 31, 2025, we were in compliance with the financial covenants and other terms of the arrangement. Our obligations under the Credit Agreement are collateralized by substantially all of our assets, including our intellectual property, but excluding certain customary and agreed upon assets.

The outstanding balances under the 2023 Notes bear interest at a floating annual rate equal to the greater of 5.5% above the Wall Street Journal prime rate or 13.25%. On and prior to September 30, 2024, 6.0% of the interest was payable in kind and added to the outstanding principal amount of the 2023 Notes. Monthly principal payments of 1.5% of the aggregate outstanding principal balance, including accrued PIK interest, were originally scheduled to commence on September 30, 2026. Under the terms of the Credit Agreement, we had the right to extend the first principal payment date to September 30, 2027, provided that certain financing milestones defined in the Credit Agreement were achieved on or prior to September 30, 2026. Having achieved those milestones during 2024, we exercised that election, and principal payments are now scheduled to commence on September 30, 2027. In addition, upon any principal payment, we are required to make an additional payment to the 2023 Lenders of a 6.0% fee (the “Exit Fee”) of the principal and accrued PIK interest paid. The aggregate Exit Fee of the 2023 Notes is equal to 6.0% of the total commitment of \$45.0 million plus all accrued PIK interest. All remaining outstanding principal balance, accrued interest and Exit Fee on the 2023 Notes shall be due and payable on the maturity date of September 7, 2028.

As of December 31, 2025, the balance of the 2023 Notes was carried at its fair value of \$30.6 million.

S-3 Registration Statement

On March 3, 2025, we filed a Registration Statement on Form S-3 with the U.S. Securities and Exchange Commission (“SEC”), which was subsequently amended on March 13, 2025 (as amended, the “S-3 Registration Statement”). The S-3 Registration Statement became effective on March 18, 2025. It contains a base prospectus, which covers the offering, issuance and sale of up to \$300.0 million in the aggregate of the securities from time to time in one or more offerings.

At-The-Market Offering

On March 3, 2025, concurrently with the filing of the S-3 Registration Statement, we entered into a sales agreement with Jefferies LLC as sales agent (the “Sales Agreement”) and filed a prospectus supplement under an at-the-market offering (the “ATM Offering”) covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$100.0 million of our common stock. As of December 31, 2025, we issued and sold 4,701,960 shares of our common stock under the ATM Offering at a weighted average price of \$1.53 per share, resulting in net proceeds of approximately \$6.8 million, after deducting commissions and offering expenses. No shares were sold under the Sales Agreement subsequent to December 31, 2025. On March 23 2026, we notified Jefferies LLC of our intention to terminate the Sales Agreement pursuant to its terms. As a result, the Sales Agreement will be terminated effective April 6, 2026 and no further sales will be made thereunder after such date.

August 2025 Offering

On August 6, 2025, we entered into an underwriting agreement with Ladenburg Thalmann & Co. Inc. (“Ladenburg”), in connection with the underwritten offering, issuance and sale by us of 19,047,619 shares of our common stock, warrants to purchase up to 19,047,619 shares of our common stock (the “Tranche A Warrants”) and warrants to purchase 19,047,619 shares of our common stock (the “Tranche B Warrants”). The combined offering price for each share of our common stock, accompanying Tranche A Warrant and accompanying Tranche B Warrant was \$1.05. The securities were issued pursuant to the S-3 Registration Statement and a related prospectus supplement filed with the SEC (the “August 2025 Offering”).

Each Tranche A Warrant has an exercise price per share of common stock equal to \$1.05, subject to certain adjustments. The Tranche A Warrants are exercisable at any time on or after August 7, 2025 and will expire on August 7, 2027. The Tranche A Warrants are callable at our option following the release of 3-month randomized midpoint clinical data from the ongoing REMAIN-1 study, which data was published on September 26, 2025, subject to satisfaction of certain conditions including that the average trading price of the stock exceeds \$1.37 per share for 15 consecutive trading days and a minimum daily trading volume threshold.

Each Tranche B Warrant has an exercise price per share of common stock equal to \$1.05, subject to certain adjustments. The Tranche B Warrants are exercisable upon receipt of the Tranche B Warrant Stockholder Approval, which was obtained at the Special Meeting of Stockholders and the Tranche B Warrants became exercisable on October 3, 2025. The Tranche B Warrants will expire on October 3, 2030, which is the date that is five years from the date of the Tranche B Warrant Stockholder Approval.

In addition, we granted Ladenburg a 30-day option to purchase up to an additional 2,857,142 shares of our common stock, along with associated Tranche A Warrants and Tranche B Warrants, at the combined public offering price of \$1.05 per share, less underwriting commissions. On August 6, 2025, Ladenburg exercised the option to purchase additional shares of our common stock, along with associated Tranche A Warrants and Tranche B Warrants, in full.

The August 2025 Offering closed on August 7, 2025, from which we received approximately \$22.6 million of net proceeds, after deducting underwriting commissions and offering expenses, excluding any potential future proceeds from the exercise of the Tranche A Warrants and Tranche B Warrants.

In December 2025, the conditions necessary to call the Tranche A warrants were satisfied and we exercised our call option. As of December 31, 2025, Tranche A Warrants were exercised to purchase 21,904,261 shares of our common stock for total proceeds of \$23.0 million, \$4.1 million of which was not received until January 2026. The remaining unexercised 500 warrants were cancelled on December 30, 2025 upon expiration of the warrant call.

As of December 31, 2025, certain holders exercised Tranche B warrants at an exercise price of \$1.05 per share resulting in the issuance of 757,759 shares of our common stock for net proceeds of \$0.8 million.

September 2025 Offering

On September 26, 2025, we entered into an underwriting agreement with BofA Securities, Inc. and Evercore Group L.L.C., as representatives of several underwriters, pursuant to which we issued and sold 60,000,000 shares of our common stock, at

a price to the public of \$1.00 per share. The securities were issued pursuant to the S-3 Registration Statement and a related prospectus supplement filed with the SEC (the “September 2025 Offering”).

The September 2025 Offering closed on September 29, 2025, from which we received approximately \$56.0 million of net proceeds, after deducting underwriting commissions and offering expenses.

Funding Requirements and Going Concern

Our future success is dependent on our ability to develop product candidates, generate significant revenue, and upon our ability to attain profitable operations. We are subject to a number of risks similar to other early-stage life science companies, including, but not limited to, successful discovery and development of our product candidates, raising additional capital with favorable terms, development by our competitors of new technological innovations, protection of proprietary technology and market acceptance of our products. The successful discovery and development of product candidates requires substantial capital which may not be available to us on favorable terms or not at all.

To date, we have financed our operations primarily through our equity and debt financings. We have a history of operating losses and had an accumulated deficit of \$556.3 million as of December 31, 2025. Management believes that our available cash and cash equivalents of \$81.5 million as of December 31, 2025, combined with \$4.1 million subsequent proceeds received in January 2026 from the Tranche A warrant exercises, will be sufficient to fund our operating expenses and capital expenditure requirements into early 2027, through multiple key clinical and regulatory milestones. Our estimate as to how long we expect our existing cash and cash equivalents will be able to continue to fund our operating expenses and capital expenditure requirement is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. In addition, without additional financing, we may not be able to comply with the minimum liquidity covenant related to our 2023 Notes by the end of 2026. Given the inherent risk and uncertainty of future cash flow estimates as well as the minimum liquidity covenant requirement, we have concluded that substantial doubt exists about our ability to continue as a going concern for at least 12 months from the issuance date of this Annual Report on Form 10-K. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

We expect to seek additional funds through equity or debt financings or through collaboration or licensing transactions or other sources. We may be unable to obtain equity or debt financings or enter into collaboration or licensing transactions and, if necessary, we will be required to implement cost reduction strategies which could curtail or delay our current operating plans.

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; 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 U.S. or elsewhere. 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 pandemics, monetary policy changes, 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 Part I, Item 1A, “Risk Factors—Risks Related to Our Financial Condition and Capital Requirements.”

We will require substantial additional capital beyond the proceeds received from our prior financings to fund 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

The net change in cash, cash equivalents and restricted cash for the years ended December 31, 2025 and 2024 was as follows:

(in thousands)	Year Ended December 31,	
	2025	2024
Net cash used in operating activities	\$ (90,328)	\$ (65,521)
Net cash used in investing activities	(557)	(1,765)
Net cash provided by financing activities	104,961	101,226
Net increase in cash, cash equivalents and restricted cash	<u>\$ 14,076</u>	<u>\$ 33,940</u>

Operating Activities

Cash used in operating activities of \$90.3 million for the year ended December 31, 2025 was primarily driven by spending on our ongoing clinical studies, Rejuva-related research activities, professional services related to our corporate and general administrative activities, as well as personnel-related expenses, including salaries, bonuses, and other compensatory benefits. Cash used in operating activities resulted primarily from our net loss of \$141.0 million adjusted for net non-cash loss of \$51.0 million, primarily consisting of \$40.9 million non-cash loss from changes in the fair value of warrant liabilities, \$0.4 million non-cash loss from change in fair value of notes payable, \$6.7 million stock-based compensation expense, \$1.6 million non-cash operating lease expense, \$1.1 million depreciation expense and \$0.3 million non-cash interest expense. Cash used in operating activities was also impacted by changes in working capital and other assets and liabilities of \$0.4 million.

Cash used in operating activities of \$65.5 million for the year ended December 31, 2024 was primarily driven by spending on Revita and Rejuva clinical and preclinical activities, professional services related to our corporate and general administrative activities, as well as personnel-related expenses, including salaries, bonuses, and other compensatory benefits. Cash used in operating activities resulted primarily from our net loss of \$68.7 million adjusted to exclude net non-cash income of \$6.4 million, primarily consisting of \$17.9 million non-cash gain from change in fair value of warrant liabilities and \$5.8 million non-cash gain from change in fair value of notes payable, offset by \$14.4 million in stock-based compensation, \$1.9 million non-cash operating lease expense, \$0.7 million depreciation and \$0.3 million non-cash interest expense. Cash used in operating activities was also impacted by changes in working capital and other assets and liabilities of \$9.6 million.

Investing Activities

Cash used in investing activities for the years ended December 31, 2025 and 2024 was related to the purchase of property and equipment. The decrease in the year ended December 31, 2025 as compared with the year ended December 31, 2024 was primarily due to our spending on leasehold improvements, office furniture and information technology equipment as we moved into our new office and laboratory space in Burlington, MA, in the first quarter of 2024.

Financing Activities

Cash provided by financing activities of \$105.0 million for the year ended December 31, 2025 was primarily driven by \$85.4 million net proceeds received from our equity offerings, including \$22.6 million from the August 2025 Offering, \$56.0 million raised from the September 2025 Offering and \$6.8 million from the ATM Offering. We also received proceeds of \$19.7 million from warrant exercises and \$0.3 million from option exercises. These financing cash inflows are partially offset by \$0.4 million principal payments made on finance lease obligations.

Cash provided by financing activities of \$101.2 million for the year ended December 31, 2024 was primarily driven by the \$103.7 million capital raised from the IPO, net of discounts and commissions, partially offset by \$2.9 million payments of public offering costs made to third-party service providers. We also received proceeds of \$0.6 million from stock option exercises. These financing cash inflows are partially offset by \$0.2 million principal payments made on finance lease obligations.

Contractual Obligations and Commitments

We have entered into arrangements that contractually obligate us to make payments that will affect our liquidity and cash flows in future periods.

As of December 31, 2025, our lease commitments reflect payments due for our operating and finance leases. The operating leases include our corporate office and laboratory space in Burlington, MA that will expire in June 2034. The finance leases represent laboratory equipment used in our Rejuva preclinical activities. As of December 31, 2025, our future contractual commitments for our leases were \$52.3 million, of which \$51.5 million were related to our operating leases. For additional information on our leases and timing of future payments, please see Note 7—“Commitments and Contingencies” to the consolidated financial statements included in this Annual Report on this Form 10-K.

We have also entered into contracts in the normal course of business with various third parties for clinical trials, preclinical research studies, manufacturing, and other services and products for operating purposes. These contracts do not contain any minimum purchase commitments and provide for termination upon notice. Payments due upon cancellation generally consist only of payments for services provided or expenses incurred, including non-cancellable obligations of our service providers, up to the date of cancellation.

Recent Accounting Pronouncements

See Note 2—“Significant Accounting Policies” to our audited consolidated financial statements for the years ended December 31, 2025 and 2024 included elsewhere in this Annual Report on Form 10-K for more information.

JOBS Act Accounting Election

We are an “emerging growth company” within the meaning of the Jumpstart Our Business Act of 2012 (“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 have also elected 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 \$1.235 billion or more; (2) the last day of our fiscal year following the fifth anniversary of the date of the completion of our IPO; (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 SEC.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company as defined in Item 10(f)(1) of Regulation S-K. As a result, pursuant to Item 305(e) of Regulation S-K, we are not required to provide the information required by this Item 7A.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Part IV, Item 15. *Exhibits and Financial Statement Schedules* of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). As part of this evaluation, management considered cybersecurity risks, including the potential for cyber incidents to affect the Company's ability to record, process, summarize, and report information required to be disclosed in our SEC filings within the required time periods. Management's assessment included consideration of the cybersecurity risk management program described in Part I, Item 1C of this Annual Report on Form 10-K, including the effectiveness of controls and procedures for identifying and escalating cybersecurity risks and incidents, and for assessing their potential impact on our financial reporting and disclosure obligations. Based on that evaluation, our principal executive officer and principal financial officer concluded that, as of December 31, 2025, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Management has assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2025, using the criteria described in Internal Control—Integrated Framework (2013 framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this evaluation, our management concluded that the Company's internal control over financial reporting was effective as of December 31, 2025.

This Annual Report on Form 10-K does not include an attestation report of our independent registered accounting firm. Our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act or even after we no longer qualify as an "emerging growth company," if we remain a "low-revenue smaller reporting company," until we are no longer a "low-revenue smaller reporting company."

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

(a) Disclosure in lieu of reporting on a Current Report on Form 8-K.

None.

(b) Insider Trading Arrangements and Policies.

During the three months ended December 31, 2025, no director or officer of the Company (as defined in Rule 16a-1(f) under the Exchange Act) adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item is incorporated by reference to the information set forth in the sections entitled “Our Board of Directors” and “Our Executive Officers” in our definitive proxy statement to be filed with the SEC on Schedule 14A in connection with our 2026 Annual Meeting of Shareholders (the “Proxy Statement”), which is expected to be filed no later than 120 days after December 31, 2025.

Our board of directors has adopted the Fractyl Health, Inc. Code of Business Conduct and Ethics that applies to all officers, directors and employees. This includes our principal executive officer, principal financial officer and principal accounting officer or controller or persons performing similar functions. The nominating and corporate governance committee is responsible for overseeing the Code of Business Conduct and Ethics and must approve any waivers of the Code of Ethics for our employees, executive officers and directors. The Code of Business Conduct and Ethics is available on our website at ir.fractyl.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to the principal executive officer, principal financial officer and principal accounting officer or controller or persons performing similar functions, we will promptly disclose the nature of the amendment or waiver on our website. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K, and you should not consider information on our website to be part of this Annual Report on Form 10-K.

Item 11. Executive Compensation.

Information required by this item is incorporated by reference to the information set forth in the sections entitled “Executive Compensation” and “Director Compensation” in the Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item is incorporated by reference to the information set forth in the sections entitled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in the Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item is incorporated by reference from the sections entitled “Certain Relationships and Related Transactions” and “Director Independence” in the Proxy Statement.

Item 14. Principal Accountant Fees and Services

Information required by this item is incorporated by reference to the information set forth in the section entitled “Independent Registered Public Accounting Firm Fees and Services” in the Proxy Statement.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements.

The following documents are included on pages F-1 through F-- attached hereto and are filed as part of this Annual Report on Form 10-K.

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(a)(2) Financial Statement Schedules.

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation of Fractyl Health, Inc.	8-K	001-41942	3.1	2/06/2024	
3.2	Amended and Restated Bylaws of Fractyl Health, Inc.	8-K	001-41942	3.2	2/06/2024	
4.1	Specimen Stock Certificate evidencing the shares of common stock.	S-1	333-276046	4.1	12/14/2023	
4.2	Fifth Amended and Restated Investors' Rights Agreement, dated June 9, 2021, by and among Fractyl Health, Inc. and certain of its stockholders.	S-1/A	333-276046	4.2	1/29/2024	
4.3	Description of Registrant's Securities	10-K	001-41942	4.3	4/1/2024	
4.4	Form of Indenture between the Registrant and one or more trustees to be named.	S-3	333-285522	4.4	3/3/2025	
4.5	Warrant Agency Agreement	8-K	001-41942	4.1	8/7/2025	
4.6	Form of Tranche B Warrant	8-K	001-41942	4.3	8/7/2025	
4.7	Form of Pre-Funded Warrant issued to entities affiliated with Nantahala Capital Management					*
10.1#	Credit Agreement and Guaranty, dated September 7, 2023, by and among Fractyl Health, Inc., Symbiotic Capital Opportunities Holding, L.P. and Catalio Structured Opportunities AIV LLP.	S-1	333-276046	10.1	12/14/2023	

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
10.2	First Amendment to Credit Agreement and Guaranty, dated October 16, 2023, by and among the Fractyl Health, Inc., Symbiotic Capital Opportunities Holding, L.P. and Symbiotic Capital Agency LLC.	S-1	333-276046	10.2	12/14/2023	
10.3	Second Amendment to Credit Agreement and Guaranty, dated December 9, 2023, by and among Fractyl Health, Inc., Symbiotic Capital Opportunities Holding, L.P. and Symbiotic Capital Agency LLC.	S-1	333-276046	10.3	12/14/2023	
10.4†	Fractyl Health, Inc. Amended and Restated 2011 Stock Incentive Plan and forms of award agreements thereunder	10-Q	001-41942	10.1	5/13/2024	
10.5†	Employment Letter Agreement, dated January 26, 2024, by and between Fractyl Health, Inc. and Harith Rajagopalan, M.D., Ph.D.	S-1/A	333-276046	10.5	1/29/2024	
10.6†	Employment Letter Agreement, dated January 26, 2024, by and between Fractyl Health, Inc. and Lisa A. Davidson	S-1/A	333-276046	10.6	1/29/2024	
10.7†	Employment Letter Agreement, dated January 26, 2024, by and between Fractyl Health, Inc. and Jay D. Caplan	S-1/A	333-276046	10.7	1/29/2024	
10.8†	Employment Letter Agreement, dated January 26, 2024, by and between Fractyl Health, Inc. and Sarah Toomey	S-1/A	333-276046	10.8	1/29/2024	
10.9	Lease Agreement, dated August 10, 2022, by and between Fractyl Health, Inc. and 3 VDG Owner LLC.	S-1	333-276046	10.11	12/14/2024	
10.10†	Fractyl Health, Inc. 2024 Incentive Award Plan and forms of award agreements thereunder					*
10.11†	Fractyl Health, Inc. 2024 Employee Stock Purchase Plan	S-1/A	333-276046	10.16	1/29/2024	
10.12†	Fractyl Health, Inc. Non-Employee Director Compensation Program	S-1/A	333-276046	10.17	1/29/2024	
10.13†	Form of Indemnification Agreement by and among Fractyl Health, Inc. and its directors and officers	S-1/A	333-276046	10.15	12/14/2023	
10.14	Form of Voting Agreement by and among the Company and its directors, its officers and Mithril, dated August 6, 2025	8-K	001-41942	10.1	8/7/2025	
10.15†	Employment Letter Agreement, dated January 26, 2024, by and between Fractyl Health, Inc. and Lara Smith Weber	8-K	001-41942	10.1	1/5/2026	
10.16†	Inducement Award Agreement between Fractyl Health, Inc. and Lara Smith Weber dated January 12, 2026	S-8	333-292715	99.3	1/13/2026	
10.17†	Separation Agreement and Release, dated December 31, 2025, by and between Fractyl Health, Inc. and Lisa Davidson	8-K	001-41942	10.2	1/6/2026	
10.18†	Consulting Agreement, dated January 1, 2026, by and between Fractyl Health, Inc. and Lisa Davidson	8-K	001-41942	10.3	1/6/2026	
10.19	Sales Agreement, dated March 3, 2025, by and between Fractyl Health, Inc. and Jefferies LLC.	S-3	333-285522	1.2	3/3/2025	
19.1	Fractyl Health, Inc. Insider Trading Compliance Policy					*

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
21.1	List of Subsidiaries	S-1	333-276046	21.1	12/14/2023	
23.1	Consent of Independent Registered Public Accounting Firm					*
24.1	Power of Attorney (incorporated by reference to the signature pages of this Annual Report on Form 10-K).					*
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer					*
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer					*
32.1	Section 1350 Certification of Chief Executive Officer and Chief Financial Officer					**
97.1	Fractyl Health, Inc. Policy for Recovery of Erroneously Awarded Compensation	10-K	001-41942	97.1	4/1/2024	
101.INS	Inline XBRL Instance Document					
101.SCH	Inline XBRL Taxonomy Extension Schema Document					
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)					

* Filed herewith

** Furnished herewith

† Indicates a management contract or compensatory plan or arrangement.

Schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant undertakes to furnish supplemental copies of any of the omitted schedules upon request by the SEC.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Fractyl Health, Inc.

Date: March 24, 2026

By: /s/ Harith Rajagopalan
Harith Rajagopalan, M.D. Ph.D.
Co-Founder, Chief Executive Officer and Director

POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Harith Rajagopalan, M.D., Ph.D. and Lara Smith Weber, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Registration Statement (including post-effective amendments), and to file the same, with 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 and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Harith Rajagopalan</u> Harith Rajagopalan, M.D., Ph.D.	Co-Founder, Chief Executive Officer and Director (Principal Executive Officer)	March 24, 2026
<u>/s/ Lara Smith Weber</u> Lara Smith Weber	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 24, 2026
<u>/s/ Kelly Barnes</u> Kelly Barnes	Director	March 24, 2026
<u>/s/ William W. Bradley</u> William W. Bradley	Director	March 24, 2026
<u>/s/ Samuel Conaway</u> Samuel Conaway	Director	March 24, 2026
<u>/s/ Marc Elia</u> Marc Elia	Director	March 24, 2026
<u>/s/ Clive Meanwell</u> Clive Meanwell, M.B., Ch.B., M.D.	Director	March 24, 2026
<u>/s/ Ajay Royan</u> Ajay Royan	Chairman	March 24, 2026
<u>/s/ Ian Sheffield</u> Ian Sheffield	Director	March 24, 2026
<u>/s/ Christopher C. Thompson</u> Christopher C. Thompson, M.D., MSc	Director	March 24, 2026

Fractyl Health, Inc.

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Report of Independent Registered Public Accounting Firm

To the Stockholders 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, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2025, 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 as of December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2025, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring operating losses and negative cash flows, expects continuing operating losses and negative operating cash flows for the foreseeable future, projects that it may not comply with the minimum liquidity covenant related to the Company's 2023 Notes without additional financing, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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. 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
March 24, 2026

Fractyl Health, Inc.
Consolidated Balance Sheets
(in thousands, except for share and per share information)

	December 31,	
	2025	2024
Assets		
Current assets:		
Cash and cash equivalents	\$ 81,540	\$ 67,464
Inventory	—	73
Prepaid expenses and other current assets	6,036	4,226
Total current assets	87,576	71,763
Restricted cash, long-term	4,255	4,255
Property and equipment, net	2,407	2,979
Right-of-use lease assets, operating	26,827	28,414
Other long-term assets	337	666
Total assets	<u>\$ 121,402</u>	<u>\$ 108,077</u>
Liabilities, convertible preferred stock and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 1,574	\$ 3,240
Accrued expenses and other current liabilities	11,651	11,579
Operating lease liabilities, current	5,104	4,956
Total current liabilities	18,329	19,775
Notes payable, long-term	30,586	30,162
Operating lease liabilities, long-term	25,956	27,382
Warrant liabilities, long-term	36,410	1,336
Other long-term liabilities	663	998
Total liabilities	111,944	79,653
Stockholders' equity:		
Preferred stock, \$0.00001 par value; 10,000,000 shares authorized at December 31, 2025 and 2024; no shares issued and outstanding at December 31, 2025 and 2024	—	—
Common stock, \$0.00001 par value; 300,000,000 shares authorized at December 31, 2025 and 2024; 153,372,044 and 48,755,451 shares issued and outstanding at December 31, 2025 and 2024, respectively	1	—
Additional paid-in capital	565,721	443,734
Accumulated deficit	(556,264)	(415,310)
Total stockholders' equity	9,458	28,424
Total liabilities and stockholders' equity	<u>\$ 121,402</u>	<u>\$ 108,077</u>

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,	
	2025	2024
Revenue	\$ —	\$ 93
Cost of goods sold	—	50
Gross profit	—	43
Operating expenses:		
Research and development	74,536	70,471
Selling, general and administrative	22,280	23,103
Total operating expenses	96,816	93,574
Loss from operations	(96,816)	(93,531)
Other income (expense), net:		
Interest income, net	1,540	4,146
Change in fair value of notes payable	(4,724)	2,830
Change in fair value of warrant liabilities	(40,901)	17,908
Other expense, net	(53)	(47)
Total other income (expense), net	(44,138)	24,837
Net loss and comprehensive loss	(140,954)	(68,694)
Accretion of dividends on convertible preferred stock	—	(1,737)
Net loss attributable to common stockholders	\$ (140,954)	\$ (70,431)
Net loss per share attributable to common stockholders, basic and diluted	\$ (1.86)	\$ (1.62)
Weighted-average number of common shares outstanding, basic and diluted	75,819,960	43,541,527

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except for 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' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2023	77,994,156	\$ 287,330	2,105,815	\$ 21,554	\$ 572	\$ (325,062)	
Exercise of common stock options	—	—	388,021	—	572	572	
Issuance of common stock from RSU vesting	—	—	604,509	—	—	—	
Conversion of convertible preferred stock upon initial public offering	(77,994,156)	(287,330)	36,343,909	—	287,330	287,330	
Issuance of common stock in initial public offering, net of underwriting commissions and offering costs	—	—	7,433,332	—	100,277	100,277	
Issuance of common stock to settle 2022 convertible notes payable	—	—	1,841,321	—	19,150	19,150	
Reclassification of warrant liability to equity upon initial public offering	—	—	—	—	425	425	
Exercise of common stock warrants	—	—	38,544	—	—	—	
Stock-based compensation expense	—	—	—	—	14,426	14,426	
Net loss	—	—	—	—	—	(68,694)	
Balance at December 31, 2024	—	\$ —	48,755,451	\$ 443,734	\$ (415,310)	\$ 28,424	
Exercise of common stock options	—	—	164,936	—	280	280	
Issuance of common stock from RSU vesting	—	—	22,500	—	—	—	
Issuance of common stock in connection with at-the-market offering, net of issuance costs of \$396	—	—	4,701,960	—	6,778	6,778	
Issuance of common stock in August 2025 offering, net of underwriting commissions and offering costs of \$413	—	—	21,904,761	—	3,749	3,749	
Issuance of common stock in September 2025 offering, net of underwriting commissions and offering costs of \$3,984	—	—	60,000,000	1	56,015	56,016	
Issuance of common stock under share purchase agreement	—	—	10,416	—	20	20	
Exercise of common stock warrants	—	—	22,662,020	—	48,461	48,461	
Exchange of common stock for pre-funded warrants	—	—	(4,850,000)	—	—	—	
Stock-based compensation expense	—	—	—	—	6,684	6,684	
Net loss	—	—	—	—	—	(140,954)	
Balance at December 31, 2025	—	\$ —	153,372,044	\$ 565,721	\$ (556,264)	\$ 9,458	

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2025	2024
Operating activities:		
Net loss	\$ (140,954)	\$ (68,694)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,129	677
Non-cash interest expense	296	357
Non-cash operating lease expense	1,587	1,869
Stock-based compensation expense	6,684	14,426
Change in fair value of warrant liabilities	40,901	(17,908)
Change in fair value of notes payable, non-cash	424	(5,840)
Changes in operating assets and liabilities:		
Accounts receivable	—	22
Inventory	73	—
Prepaid expenses and other current assets	2,248	(2,197)
Accounts payable	(1,666)	2,686
Accrued expenses and other current liabilities	414	5,654
Operating lease liabilities	(1,278)	1,098
Other long-term assets and liabilities	(186)	2,329
Net cash used in operating activities	<u>(90,328)</u>	<u>(65,521)</u>
Investing activities:		
Purchases of property and equipment	(557)	(1,765)
Net cash used in investing activities	<u>(557)</u>	<u>(1,765)</u>
Financing activities:		
Proceeds from initial public offering, net of underwriting discounts and commissions	—	103,695
Payments related to initial public offering costs	—	(2,854)
Issuance of common stock in connection with at-the-market offering, net of underwriting commissions and offering costs	6,778	—
Issuance of common stock and warrants in August 2025 public offering, net of underwriting commissions and offering costs	22,587	—
Issuance of common stock in September 2025 public offering, net of underwriting commissions and offering costs	56,016	—
Proceeds from issuance of common stock under share purchase agreement	20	—
Exercises of common stock warrants	19,737	—
Exercises of common stock options	280	572
Principal payments on finance lease obligations	(457)	(187)
Net cash provided by financing activities	<u>104,961</u>	<u>101,226</u>
Net increase in cash, cash equivalents and restricted cash	14,076	33,940
Cash, cash equivalents and restricted cash at beginning of period	71,719	37,779
Cash, cash equivalents and restricted cash at end of period	<u>\$ 85,795</u>	<u>\$ 71,719</u>
Supplemental disclosure of cash flow information:		
Interest paid	\$ 4,300	\$ 3,127
Payment for operating leases within operating activities	\$ 5,248	\$ 3,042
Non-cash investing and financing activities:		
Fair value of warrant liabilities recognized in connection with August 2025 public offering	\$ 18,838	\$ —
Reclassification of warrant liabilities into equity upon exercises	\$ 24,665	\$ —
Conversion of convertible preferred stock into common stock upon initial public offering	\$ —	\$ 287,330
Conversion of 2022 Convertible Notes into common stock upon initial public offering	\$ —	\$ 19,150
Reclassification of warrant liability to equity upon initial public offering	\$ —	\$ 425
Finance lease right-of-use asset obtained in exchange for lease liability	\$ —	\$ 1,401
Reclassification of deferred offering costs to additional paid-in capital	\$ —	\$ 3,418

The accompanying notes are an integral part of these consolidated financial statements.

Fractyl Health, Inc.
Notes to Consolidated Financial Statements

1. Nature of the Business

Fractyl Health, Inc. (the “Company” or “Fractyl”) was incorporated in Delaware on August 30, 2010 under the name MedCatalyst, Inc. The Company then changed its name to Fractyl Laboratories Inc. on January 10, 2012 and subsequently to Fractyl Health, Inc. on June 9, 2021. The Company is a clinical stage metabolic therapeutics company focused on pioneering novel approaches to treat obesity and T2D. The Revita[®] and Rejuva[®] candidates are designed to target root causes of metabolic diseases, allowing us to advance metabolic disease treatment from chronic management towards prevention and reversion of the disease.

Revita

The Revita DMR System (“Revita”) is based on the Company’s insights surrounding the potential role of the gut in obesity. Revita is designed to remodel the duodenal lining via hydrothermal ablation (i.e. duodenal mucosal resurfacing) to reverse damage to intestinal nutrient sensing and signaling mechanisms caused by chronic high-fat and high-sugar diets that are a root cause of metabolic disease. In the U.S., Revita is for investigational use only. Revita has U.S. FDA Breakthrough Device designation in weight maintenance for people with obesity who discontinue glucagon-like peptide-1 (“GLP-1”) based drugs. The Company has received favorable FDA feedback on its De Novo classification request for Revita and anticipate submitting a potential De Novo marketing application in the late fourth quarter of 2026. The Company is evaluating Revita in the REMAIN-1 weight maintenance program, which is designed to evaluate Revita’s potential to maintain weight loss following GLP-1 based therapy discontinuation. The REMAIN-1 program includes three distinct patient cohorts that are conducted under a single IDE: the REVEAL-1 Cohort, the REMAIN-1 Midpoint Cohort, and the REMAIN-1 Pivotal Cohort, designed to collectively establish the clinical and regulatory foundation for Revita in weight maintenance.

- The REVEAL-1 Cohort (n=22) is an open-label study in individuals with obesity who have lost at least 15% of their total body weight on a GLP-1 medication and who either need or choose to discontinue GLP-1 therapy.
- The REMAIN-1 Midpoint Cohort (n=45) is a randomized, double-blind, sham-controlled pilot study to assess the potential of Revita to maintain weight loss after GLP-1 based therapy discontinuation.
- The REMAIN-1 Pivotal Cohort (n=315) is a randomized, double-blind, sham-controlled pivotal study to evaluate the safety and efficacy of Revita in maintaining weight loss.

The REMAIN-1 study was initiated in the third quarter of 2024. The Company completed enrollment of the REMAIN-1 Pivotal Cohort in July 2025, a randomized, double-blind, sham-controlled pivotal study evaluating the safety and efficacy of Revita in maintaining weight loss after GLP-1 based therapy discontinuation. The Company completed randomization of the pivotal cohort in February 2026, with topline six-month data anticipated in the early fourth quarter of 2026. The Company anticipates submitting a potential De Novo marketing application in post-GLP-1 weight maintenance in the late fourth quarter of 2026.

Pursuant to the Company’s Strategic Reprioritization in January 2025, Fractyl has paused additional investment in the REVITALIZE-1 clinical study of Revita for T2D and the Germany Real-World Registry study. The Company continues to follow existing participants in both studies per protocol and will report clinical, health economic, and patient-relevant outcomes from the Germany Real-World Registry study on an ongoing basis.

Rejuva

The Company is also developing Rejuva, a novel, locally administered, adeno-associated virus (“AAV”) delivered pancreatic gene therapy platform. Rejuva is designed to enable long-term remission of T2D and obesity by durably reprogramming pancreatic islet cells to endogenously produce metabolic hormones. Rejuva leverages advanced delivery systems and proprietary screening methods to identify and develop metabolically active gene therapy candidates targeting the pancreas. The lead candidate from the Rejuva platform, RJVA-001 is designed to be delivered to the pancreas via a single endoscopic intervention to enable pancreatic beta cells to express GLP-1 locally via nutrient-responsive control. This gene therapy approach enables physiologic GLP-1 secretion without the high circulating levels that contribute to side effects seen with systemic GLP-based drugs. The Company completed key preclinical *in vivo* studies to support a CTA for RJVA-001 and subsequently submitted CTAs for RJVA-001 in T2D to regulators in the EU (Netherlands) and Australia in

the second half of 2025, advancing the program toward its anticipated first-in-human study. The Company expects to receive regulatory feedback in the second quarter of 2026 and, subject to CTA authorization, initiate first-in-human dosing of RJVA-001 and expected reporting of preliminary data in the second half 2026.

The Company is also developing RJVA-002, a dual GIP/GLP-1 gene therapy and is currently in preclinical development. RJVA-002 expands the Rejuva platform into obesity, targeting dual incretin biology with the goal of achieving durable, well-tolerated, weight loss from a single intervention.

The Company believes Revita and Rejuva, if approved by relevant regulatory bodies, have the potential to revolutionize treatment across the spectrum of obesity and T2D, align the clinical and economic interest of key stakeholders around the long-term regression of metabolic disease, and, at their fullest potential, significantly reduce the burden of metabolic disease globally.

Initial Public Offering (“IPO”)

On February 6, 2024, the Company completed its IPO, pursuant to which it issued and sold 7,333,333 shares of its common stock at a price to the public of \$15.00 per share, resulting in net proceeds of approximately \$98.9 million, after deducting the underwriting commissions and related offering expenses.

On March 5, 2024, the Company issued an additional 99,999 shares of its common stock pursuant to the partial exercise of the underwriters’ option to purchase additional shares at the IPO public price of \$15.00 per share, resulting in additional net proceeds of approximately \$1.4 million, after deducting the underwriting commissions.

S-3 Registration Statement

On March 3, 2025, the Company filed a Registration Statement on Form S-3 with the U.S. Securities and Exchange Commission (“SEC”), which was subsequently amended on March 13, 2025 (as amended, the “S-3 Registration Statement”). The S-3 Registration Statement became effective on March 18, 2025. It contains a base prospectus, which covers the offering, issuance and sale of up to \$300.0 million in the aggregate of the securities from time to time in one or more offerings.

At-The-Market Offering

On March 3, 2025, concurrently with the filing of the S-3 Registration Statement, the Company entered into a sales agreement with Jefferies LLC as sales agent (the “Sales Agreement”) and filed a prospectus supplement under an at-the-market offering (the “ATM Offering”) covering the offering, issuance and sale of up to a maximum aggregate offering price of \$100.0 million of the Company’s common stock. As of December 31, 2025, the Company issued and sold 4,701,960 shares of its common stock under the ATM Offering at a weighted average price of \$1.53 per share, resulting in net proceeds of approximately \$6.8 million, after deducting commissions and offering expenses. No shares were sold under the Sales Agreement subsequent to December 31, 2025. On March 23, 2026, the Company notified Jefferies LLC of its intention to terminate the Sales Agreement pursuant to its terms. As a result, the Sales Agreement will be terminated effective April 6, 2026 and no further sales will be made thereunder after such date.

August 2025 Offering

On August 6, 2025, the Company entered into an underwriting agreement with Ladenburg Thalmann & Co. Inc. (“Ladenburg”), pursuant to which it issued and sold 19,047,619 shares of its common stock, accompanied by warrants to purchase up to 19,047,619 shares of its common stock (the “Tranche A Warrants”) and warrants to purchase 19,047,619 shares of its common stock (the “Tranche B Warrants”), at a combined offering price of \$1.05 per share. As part of the underwriting agreement, the Company also granted Ladenburg a 30-day option to purchase up to an additional 2,857,142 shares of the Company’s common stock, along with associated Tranche A Warrants and Tranche B Warrants, at the combined public offering price of \$1.05 per share. On August 6, 2025, Ladenburg exercised the option to purchase additional shares of the Company’s common stock, along with associated Tranche A Warrants and Tranche B Warrants, in full. The securities were issued pursuant to the S-3 Registration Statement and a related prospectus supplement filed with the SEC (the “August 2025 Offering”).

The August 2025 Offering closed on August 7, 2025, from which the Company received approximately \$22.6 million of net proceeds, after deducting underwriting commissions and offering expenses, excluding any potential future proceeds from the exercise of the Tranche A Warrants and Tranche B Warrants. See Note 8—“Warrant Liabilities” for more details

on the Tranche A Warrants and Tranche B Warrants.

September 2025 Offering

On September 26, 2025, the Company entered into an underwriting agreement with BofA Securities, Inc. and Evercore Group L.L.C., as representatives of several underwriters, pursuant to which it issued and sold 60,000,000 shares of its common stock, at a price to the public of \$1.00 per share. The securities were issued pursuant to the S-3 Registration Statement and a related prospectus supplement filed with the SEC (the “September 2025 Offering”).

The September 2025 Offering closed on September 29, 2025, from which the Company received approximately \$56.0 million, after deducting underwriting commissions and offering expenses.

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 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 Company has a history of operating losses and had an accumulated deficit of \$556.3 million as of December 31, 2025. Management expects continuing operating losses in the future. The Company has financed its operations to date primarily through its equity and debt financings. Based on its current business plans, the Company believes that its available cash and cash equivalents of \$81.5 million as of December 31, 2025, combined with \$4.1 million subsequent proceeds received in January 2026 from the Tranche A warrant exercises, will be sufficient to fund the Company’s operating plan into early 2027. The Company’s forecast of its cash needs is subject to significant assumptions, which could change, and management could use its available capital resources sooner than it currently anticipates. In addition, without additional financing, management projects that it may not be able to comply with the minimum liquidity covenant related to the Company’s 2023 Notes by the end of 2026.

Given the inherent risk and uncertainty of future cash flow estimates as well as the minimum liquidity covenant requirement, management has concluded that substantial doubt exists about the Company’s ability to continue as a going concern for at least one year after the date that these financial statements are issued. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

The Company plans to alleviate the substantial doubt about its ability to continue as a going concern by seeking additional funds through equity or debt financings or through collaboration or licensing transactions or other sources. The Company may be unable to obtain equity or debt financings or enter into collaboration or licensing transactions and, if necessary, the Company will be required to implement cost reduction strategies which could curtail or delay its current operating plans.

2. Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles (“U.S. GAAP”) and include the accounts of the Company and its wholly owned subsidiary. Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”). All intercompany balances and transactions have been eliminated. These consolidated financial statements, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair presentation of the Company’s financial position and results of operations for the years ended December 31, 2025 and 2024.

Use of Estimates

The preparation of financial statements in conformity with U.S. 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 warrants, the fair value of notes payable, the fair value of stock-based awards, the incremental borrowing rate for lease accounting, estimates of future cash flows used in the assessment of our ability to continue as a going concern, 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.

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’s restricted cash primarily represented cash held in separate collateral bank accounts in conjunction with the maintenance of letters of credit required under the Company’s facility leases. See Note 7—“Leases” for more information on the Company’s facility leases. The letter of credit was issued for an original effective period of 12 months with automatic annual renewal until the expiration date.

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. As of December 31, 2025, substantially all of the Company’s cash and cash equivalents were maintained at two financial institutions. The Company’s deposits at times may significantly exceed federally insured limits. Potential failure of either financial institution could impact access to our cash and cash equivalents and could adversely impact our operating liquidity and financial performance. To date, the Company has not experienced any losses related to its cash and cash equivalents.

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’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 U.S. See Note 15—“Segment Information” for additional information about the Company’s segment information.

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:

<u>Asset Category</u>	<u>Estimated Useful Life</u>
Computer equipment.....	3 years
Furniture and fixtures.....	5 years
Laboratory and engineering equipment.....	3 years
Manufacturing equipment.....	5 years
Website development costs.....	3 years
Leasehold improvements.....	Shorter of remaining lease term or 7 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 and finance 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.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under U.S. 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, notes payable, and warrant liabilities are carried at fair value, determined according to the fair value hierarchy above. See Note 3—"Fair Value Measurements" for additional detail on these fair value measurements. 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.

Leases

The Company applies the provisions of ASC 842, *Leases*, (“ASC 842”) to account for its operating leases for office and laboratory spaces and finance leases for certain laboratory equipment.

The Company determines whether an arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement at inception. Operating leases are included in right-of-use lease assets (“ROU assets”) and current and long-term lease liabilities on the Company’s consolidated balance sheets. Lease expenses for operating leases are recognized on a straight-line basis over the lease term as an operating expense. Assets subject to finance leases are included in property and equipment, net, on the Company’s consolidated balance sheets. Current and long-term portion of the related lease liabilities of the finance leases are included in accrued expenses and other current liabilities and other long-term liabilities, respectively, on the Company’s consolidated balance sheets. Lease expenses for finance leases consist of depreciation of the assets, which is recognized on a straight-line basis over the useful life of the assets as an operating expense, and interest expense using the effective interest method over the lease term.

At the lease commencement date, the Company recognizes an ROU asset and a lease liability based on the present value of fixed lease payments over the expected lease term. 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. Certain adjustments to the ROU 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 has elected the short-term lease recognition exemption for short-term leases, which allows the Company not to recognize lease liabilities and ROU assets on the consolidated balance sheets for leases with an original lease term of twelve months or less. Rent expenses for short-term leases are directly expensed as operating expenses in the consolidated statements of operations and comprehensive loss.

The Company has elected to not separate lease and non-lease components. Only the fixed costs for lease components and their associated non-lease components are accounted for as a single lease component and recognized as part of the ROU asset and lease liability. Variable lease costs such as taxes, operating expenses and other expenses are based on actual costs incurred and are directly expensed as operating expenses in the consolidated statements of operations and comprehensive loss.

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.

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.

Notes Payable

The Company elected to apply the fair value option ("FVO") to its notes payable in accordance with ASC 825, *Financial Instruments* ("ASC 825"). Accordingly, the notes payable are re-measured at the end of each reporting period with changes in fair value recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. Changes in fair value resulting from changes in instrument-specific credit risk, if any, will be recognized separately in other comprehensive income. The primary reason for electing the fair value option was to address simplification and cost-benefit considerations that result from accounting for hybrid financial instruments at fair value in their entirety versus bifurcation of the embedded derivatives from the debt hosts.

The fair values of the notes payable are determined using valuation models that incorporate assumptions and estimates. The Company assesses these assumptions and estimates at each financial reporting period as additional information impacting the assumptions is obtained. Assumptions in the models include but are not limited to equity value, volatility, time to conversion event, risk-free rate, scenario weightings and observable market yields for similarly rated instruments. The fair value measurements of the notes payable are based on significant inputs that are not observable in the market and represent a Level 3 measurement. See Note 6—"Notes Payable."

Warrant Liabilities

The Company classifies warrants to purchase shares of its common stock as liabilities on its consolidated balance sheets as such warrants may result in delivery of variable number of shares or delivery of a settlement amount that is not solely indexed to the Company's own stock. These warrants were initially recorded at fair value on the grant date, and are subsequently remeasured to fair value at the end of each reporting period and at exercise with changes in fair value recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. The Company will continue to adjust the liabilities until the earlier of exercise or expiration of the warrant.

The fair values of these warrant liabilities are determined using either a Black-Scholes option-pricing model or a Monte Carlo simulation model, depending on the nature of the warrants. The valuation model used incorporates assumptions and estimates, which the Company assesses 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 shares, the remaining contractual term of the warrants, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying shares. The fair value of the underlying shares represents the closing price of its common stock traded on the Nasdaq Global Market. The Company was historically a private company until its IPO in February 2024, and lacked company-specific historical and implied volatility information of its stock. Therefore, it estimated 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 warrants and expects to continue to consider peer company volatility until such time as it has adequate historical data regarding the volatility of its own traded stock price. 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 for the common stock warrants is 0% based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends on common stock in the foreseeable future.

This fair value measurement of the warrant liabilities is based on significant inputs that are not observable in the market and represent a Level 3 measurement. See Note 8—"Warrant Liabilities."

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 is 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 recognized using an accelerated attribution method. Upon final determination of the performance conditions achieved, the compensation costs are adjusted to reflect those awards that ultimately vest. Historical performance patterns, to the extent that they are indicative of 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 considers the fair value of its common stock to be equal to the closing price of its common stock traded on the Nasdaq Global Market. Due to the limited company-specific historical and implied volatility information available to the Company, the expected stock volatility used in the option pricing model was 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 0% 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' equity 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, 2025 and 2024.

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. 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 stock option awards and outstanding warrants to purchase common stock were anti-dilutive. See Note 14—"Net Loss Per Share" for additional information.

Emerging Growth Company Status

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act ("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 December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"). The ASU focuses on the rate reconciliation and income taxes paid. ASU 2023-09 requires the Company to disclose, on an annual basis, a tabular rate reconciliation using both percentages and currency amounts, broken out into specified categories with certain reconciling items further broken out by nature and jurisdiction to the extent those items exceed a specified threshold. ASU 2023-09 is effective for annual periods beginning after December 15, 2024, with early adoption permitted. The Company elected to adopt ASU 2023-09 effective January 1, 2025 on a prospective basis. See Note 12—"Income Taxes," for further disclosure.

Recently Issued Accounting Pronouncements

In November 2024, the FASB issued ASU No. 2024-03, *Disaggregation of Income Statement Expenses* ("ASU 2024-03"), which is intended to provide more detailed and disaggregated information about significant expense categories, such as purchases of inventory, employee compensation, depreciation and amortization and selling expenses. This new standard, including related updates, is effective for fiscal years beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted, and the amendments may be applied either prospectively or retrospectively. The Company is currently assessing the impact ASU 2024-03 will have on its consolidated financial statements, including our footnote disclosures.

In September 2025, the FASB issued ASU No. 2025-06, *Intangibles - Goodwill and Other- Internal-Use Software (Subtopic 350-40): Targeted Improvements to the Accounting for Internal-Use Software* ("ASU 2025-06"). The ASU simplifies the guidance around capitalization of software development costs. ASU 2025-06 is effective for annual periods beginning December 31, 2027, with early adoption permitted. The Company plans to early adopt ASU 2025-06 effective January 1, 2026. The Company is currently evaluating the impact that adoption of the standard will have on its consolidated 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:

(in thousands)	Fair Value Measurements as of December 31, 2025			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents—money market funds	\$ 35,829	\$ —	\$ —	\$ 35,829
	<u>\$ 35,829</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 35,829</u>
Liabilities:				
Warrant liabilities, long-term	\$ —	\$ —	\$ 36,410	\$ 36,410
Notes payable, long-term	—	—	30,586	30,586
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 66,996</u>	<u>\$ 66,996</u>

(in thousands)	Fair Value measurements as of December 31, 2024			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents—money market funds	\$ 38,295	\$ —	\$ —	\$ 38,295
	<u>\$ 38,295</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 38,295</u>
Liabilities:				
Warrant liabilities, long-term	\$ —	\$ —	\$ 1,336	\$ 1,336
Notes payable, long-term	—	—	30,162	30,162
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 31,498</u>	<u>\$ 31,498</u>

During the years ended December 31, 2025 and 2024, there were no transfers between Level 1, Level 2 and Level 3.

See Note 6—"Notes Payable" for the discussion of the fair value methodology of the notes payable and a rollforward of the fair value. See Note 8—"Warrant Liabilities" for the discussion of the fair value methodology of the common stock warrants and a rollforward of the fair value.

4. Property and Equipment, Net

Property and equipment, net consisted of the following:

(in thousands)	December 31,	
	2025	2024
Computer equipment	\$ 519	\$ 519
Furniture and fixture	1,237	1,237
Lab and engineering equipment	2,345	2,048
Manufacturing equipment	337	77
Website development costs	94	94
Leasehold improvements	599	599
	<u>5,131</u>	<u>4,574</u>
Less: accumulated depreciation	(2,724)	(1,595)
	<u>\$ 2,407</u>	<u>\$ 2,979</u>

Property, plant, and equipment in the table above includes leased equipment under the Company's finance leases of \$0.6 million and \$1.1 million as of December 31, 2025 and 2024, respectively. Depreciation expense for the years ended December 31, 2025 and 2024 were \$1.1 million and \$0.7 million, respectively.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

(in thousands)	December 31,	
	2025	2024
Payroll and payroll-related expenses	\$ 5,653	\$ 4,184
Research and development services	4,316	5,750
Professional fees and consulting services	721	814
Other current liabilities	961	831
	<u>\$ 11,651</u>	<u>\$ 11,579</u>

6. Notes Payable

2022 Convertible Notes

On January 11, 2022, the Company entered into a financing arrangement with certain lenders in which the Company issued convertible promissory notes in exchange for an aggregate principal amount of \$20.1 million (the “2022 Convertible Notes”). On July 11, 2023, the Company issued amended and restated convertible promissory notes to certain of the lenders (the “Continuing 2022 Lenders”) in replacement of, but not in payment of, the remainder of the 2022 Convertible Notes. Following these amendments, \$20.9 million in aggregate principal under the 2022 Convertible Notes remained outstanding and accrued interest at the rate of 10% per year until they were paid or converted in full.

In connection with entering into these amendments, the Company issued to the Continuing 2022 Lenders warrants to purchase shares of the Company’s common stock with par value of \$0.00001 per share. The warrants were recorded as part of the warrant liabilities on the consolidated balance sheets.

Upon the closing of the IPO on February 6, 2024, all of the outstanding principal plus accrued interest under the 2022 Convertible Notes were converted into 1,841,321 shares of the Company’s common stock at a conversion price of \$12.00 per share. The 2022 Convertible Notes were marked to market to their fair value as of the time of the conversion before being reclassified to equity.

2023 Notes

On September 7, 2023, the Company entered into a credit agreement (the “Credit Agreement”) with certain lenders (the “2023 Lenders”) that provided for term loans in an aggregate principal amount of \$45.0 million (the “Applicable Commitments”) in two tranches (the “2023 Notes”). The first tranche with a principal amount of \$30.0 million was extended on September 7, 2023. The second tranche with a principal amount of \$15.0 million would have been extended upon the Company’s achievement of certain operating and funding milestones, as defined in the Credit Agreement, by July 31, 2024. Under the Credit Agreement, a further principal amount of \$20.0 million may be extended to the Company, subject to the 2023 Lenders’ prior written consent in their sole discretion. Due to a shift in business strategy to include the weight maintenance study, the Company decided not to pursue the milestones required to access the second tranche. As a result, the second tranche was not extended.

The outstanding balances of the 2023 Notes bear interest at a floating annual rate equal to the greater of 5.5% above the Wall Street Journal prime rate or 13.25%. On and prior to September 30, 2024, 6.0% of the interest was payable in kind (the “PIK interest”) and added to the outstanding principal amount of the loans. Beginning September 30, 2026, the Company is required to make monthly principal payments in the amount of 1.5% of the aggregate principal amount outstanding, including accrued PIK interest. The Credit Agreement permits a one year extension of the commencement date to September 30, 2027, at the Company’s option if specified financing milestones are achieved by September 30, 2026. In 2024, the Company met these milestones and elected to extend the commencement date to September 30, 2027. In addition, upon any principal payment, the Company is required to make an additional payment to the 2023 Lenders of a 6.0% fee (the “Exit Fee”) over the principal and accrued PIK interest paid. The aggregate Exit Fee of the 2023 Notes should be equal to 6.0% of the total Applicable Commitments of \$45.0 million plus all accrued PIK interest. All remaining outstanding principal balance, accrued interest and Exit Fee on the 2023 Notes shall be due and payable on the maturity date of September 7, 2028.

In connection with the issuance of the first tranche of the 2023 Notes, the Company issued to the 2023 Lenders warrants to purchase, at the holders' choice, shares of the Company's Series F Convertible Preferred Stock, the most senior series of Preferred Stock of the Company that was then authorized, or the Company's common stock. The warrants were recorded as part of the warrant liabilities on the consolidated balance sheets.

The Company elected to apply the FVO to the 2023 Notes in accordance with ASC 825, *Financial Instruments*. Accordingly, the 2023 Notes are marked to market at the end of each reporting period, with changes in fair value recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. The fair value was estimated using a discounted cash flow model by discounting projected future cash flows associated with the 2023 Notes to their present value. The discount rate used in the model is based on observable market yields for similarly rated instruments, adjusted for any specific risks inherent in the 2023 Notes, which is a level 3 fair value measurement and requires judgment to determine at each period end. Accrued interest on the 2023 Notes is incorporated into the determination of the fair value of the 2023 Notes.

This fair value measurement is based on significant inputs that are not observable in the market and represent a Level 3 measurement. The following table provides a roll forward of the fair value of the 2023 Notes:

(in thousands)	<u>Fair Value</u>
Balance as of December 31, 2024	\$ 30,162
Change in fair value	4,724
Payment of interest	<u>(4,300)</u>
Balance as of December 31, 2025	<u>\$ 30,586</u>

The Credit Agreement contains a minimum liquidity covenant that requires the Company to maintain a \$10.0 million minimum balance in cash and/or certain permitted cash equivalent investments, subject to certain exceptions. In addition, the Credit Agreement contains a customary events of default, subject to rights and remedies generally applicable to federal law or the laws of the State of Delaware. As of December 31, 2025, the Company was in compliance with the financial covenants and other terms of the arrangement. The Company's obligations under the Credit Agreement are collateralized by substantially all of its assets, including its intellectual property, but excluding certain customary and agreed upon assets.

7. Leases

Lexington Lease

In November 2015, the Company entered into a lease agreement for 30,000 square feet of office and laboratory space in Lexington, Massachusetts (the "Lexington Lease") with an initial lease term covering a seven-year period from May 1, 2016 through April 30, 2023. In June 2022, the Company extended the initial term of the Lexington Lease for twelve months. The Lexington Lease expired on April 30, 2024 at the end of its extended term.

Burlington Lease

In August 2022, the Company entered into a lease agreement for 78,000 square feet of office and laboratory space in Burlington, Massachusetts (the "Burlington Lease"). The lease contains a total lease term of 128 months, which includes an initial eight-month period of free rent and a remaining lease term of 10 years. Total lease payments for the Burlington Lease amount to \$59.3 million. Additionally, the Burlington Lease incorporates a five-year renewal option exercisable at the Company's discretion; however, these extensions were not included in the operating lease assets and lease liabilities recorded on the consolidated balance sheets as they were not reasonably certain of being exercised.

The Burlington Lease commenced on November 1, 2023, upon which the Company recognized the right-of-use asset and lease liability of \$30.2 million on its consolidated balance sheet in accordance with ASC 842. The Company estimated the incremental borrowing rate at the time of the Burlington Lease commencement to be 12.67%, which was used as the discount rate in the measurement of the lease liabilities.

The following table is a summary of the components of operating lease expenses for the years ended December 31, 2025 and 2024:

(in thousands)	2025	2024
Operating lease cost	\$ 5,548	\$ 5,934
Short-term lease cost	13	138
Variable lease cost	682	1,393
Total lease cost	<u>\$ 6,243</u>	<u>\$ 7,465</u>

The Company's operating leases require payments for certain operating expenses, taxes, and other expenses based on actual costs incurred. As these amounts are variable in nature, these payments are expensed in the periods incurred and included in variable lease costs for the years ended December 31, 2025 and 2024.

The weighted-average remaining lease term and weighted-average discount rate for the Company's operating leases as of December 31, 2025 and 2024 were as follows:

	2025	2024
Weighted-average remaining lease term in years	8.5	9.5
Weighted-average discount rate	12.7%	12.7%

The following table summarizes the maturity of operating lease liabilities as of December 31, 2025:

Year Ending December 31, (in thousands)	
2026	\$ 5,406
2027	5,568
2028	5,735
2029	5,907
2030	6,084
Thereafter	22,776
Total future minimum lease payments	<u>51,476</u>
Less: Imputed interest	<u>(20,416)</u>
Total lease liabilities	<u>\$ 31,060</u>

Future minimum operating lease payments above do not include those committed under short-term leases and leases not yet commenced.

The Company has an obligation to maintain a letter of credit as the security deposit for its Burlington Lease, which is held in favor of the lessor. This letter of credit was initially issued for a period of 12 months with automatic annual renewal until the expiration date specified in the lease agreement. As of December 31, 2025, the Company had a total of \$4.3 million outstanding in the letter of credit associated with the Burlington Lease, which was collateralized by cash maintained in a collateral bank account. The balance of the cash maintained in the collateral bank account has been included in restricted cash, long-term, on the Company's consolidated balance sheet.

8. Warrant Liabilities

2014 Warrant

In January 2014, the Company issued a fully vested warrant to purchase 118,483 shares of the Company's Series B Convertible Preferred Stock (the "2014 Warrant") in connection with a loan and security agreement entered into in January 2014. The 2014 Warrant was immediately exercisable at an exercise price of \$1.266 per share and has a contractual term of ten years from issuance. In January 2024, the 2014 Warrant was amended to extend the expiration date to the earlier of (i) the date that is 30 calendar days after the closing of the Company's IPO and (ii) July 31, 2024. Upon the closing of the Company's IPO on February 6, 2024, the amended expiration date of the 2014 Warrant was determined to be March 7, 2024.

The Company remeasured the fair value of the 2014 Warrant at the end of each reporting period, with any adjustments

recorded as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. Upon the closing of the IPO on February 6, 2024, the warrant to purchase 118,483 shares of the Company’s Series B Convertible Preferred Stock was converted to a warrant to purchase 55,211 shares of the Company’s common stock. Accordingly, the 2014 Warrant was remeasured upon the closing of the IPO and marked to market to its fair value before being reclassified to equity.

The 2014 Warrant was fully cashless exercised on the amended expiration date of March 7, 2024, as a result of which a total of 38,544 shares of common stock were issued to the warrant holder.

July 2023 Warrants

In July 2023, the Company issued fully vested warrants to purchase shares of the Company’s common stock in connection with the issuance of the amended and restated 2022 Convertible Notes (the “July 2023 Warrants”). The July 2023 Warrants were immediately exercisable for a variable number of shares based on the principal amount of the 2022 Convertible Notes, as amended, of \$20.9 million, and an exercise price, at the holders’ choice, of (a) \$17.9927 per share, (b) the lowest original issue price of shares of Preferred Stock of the Company issued in the Company’s next bona fide private preferred equity financing round, (c) in the event of any convertible note or similar convertible security financing, the conversion price contemplated by such convertible security, or (d) in the event of an IPO, the per share offering price to the public in such IPO. The July 2023 Warrants have a contractual term of ten years from issuance. They were not exercised from their inception through December 31, 2025.

The fair value of the July 2023 Warrants was recorded as part of the warrant liabilities on the consolidated balance sheets. The Company remeasures the fair value at the end of each reporting period, with any adjustments being recorded as a component of other income (expense) in the consolidated statements of operations and comprehensive loss.

The fair value of the July 2023 Warrants was determined using the Black-Scholes valuation model with the following assumptions:

	December 31,	
	2025	2024
Risk-free interest rate	3.9%	4.5%
Expected term (in years)	7.5	8.5
Expected volatility	60%	59%
Expected dividend yield	0%	0%

The following table provides a rollforward of the fair value of the July 2023 Warrants:

(in thousands)	Fair Value
Balance as of December 31, 2024	\$ 1,169
Change in fair value	(30)
Balance as of December 31, 2025	<u>\$ 1,139</u>

September 2023 Warrants

In September 2023, in connection with the issuance of the 2023 Notes, the Company issued fully vested warrants to purchase, at the holders’ choice, shares of the Company’s Series F Convertible Preferred Stock, the most senior series of Preferred Stock of the Company that was then authorized, or the Company’s common stock (the “September 2023 Warrants”). The September 2023 Warrants are immediately exercisable for a variable number of shares based on a total fixed dollar value of \$4.2 million, and an exercise price, at the holders’ choice, of (a) \$17.9927 per share of common stock or \$8.3843 per share of Series F Convertible Preferred Stock, (b) the lowest original issue price of any series of Preferred Stock issued by the Company after the issuance date of the September 2023 Warrants, (c) the conversion or exercise price of any convertible debt security, option, or warrant issued by the Company after the issuance date of the September 2023 Warrants, or (d) the price at which the Company’s common equity was first sold to the public by the Company in a firm-commitment underwritten offering or otherwise. The September 2023 Warrants have a contractual term of ten years from issuance. They were not exercised from their inception through December 31, 2025.

The fair value of the September 2023 Warrants was recorded as part of the warrant liabilities on the consolidated balance sheets. The Company remeasures the fair value at the end of each reporting period, with any adjustments being recorded as a component of other income (expense) in the consolidated statements of operations and comprehensive loss.

The fair value of the September 2023 Warrants was determined using the Black-Scholes valuation model with the following assumptions:

	December 31,	
	2025	2024
Risk-free interest rate	4.0%	4.5%
Expected term (in years)	7.7	8.7
Expected volatility	61%	58%
Expected dividend yield	0%	0%

The following table provides a rollforward of the fair value of the September 2023 Warrants:

(in thousands)	Fair Value
Balance as of December 31, 2024	\$ 167
Change in fair value	—
Balance as of December 31, 2025	<u>\$ 167</u>

August 2025 Warrants

On August 7, 2025, the Company issued Tranche A Warrants and Tranche B Warrants to purchase 21,904,761 shares of the Company's common stock, respectively, in connection with the August 2025 Offering. See Note 1—"Nature of the Business" for more detail on the Tranche A Warrants and Tranche B Warrants. The Tranche A Warrants were immediately exercisable and the Tranche B Warrants were only exercisable upon receipt of required stockholder approval, which approval was received on October 3, 2025. See details of each set of warrants below.

August 2025 Tranche A Warrants ("Tranche A Warrants")

Each Tranche A Warrant had an exercise price of \$1.05 per share, subject to certain adjustments. The Tranche A Warrants were exercisable at any time on or after August 7, 2025 and any unexercised Tranche A Warrants were set to expire on August 7, 2027. The Tranche A Warrants were callable at the Company's option following the release of 3-month randomized midpoint clinical data from the ongoing REMAIN-1 study, which data was published on September 26, 2025, subject to satisfaction of certain conditions including that the average trading price of the Company's common stock exceeds \$1.37 per share for 15 consecutive trading days and a minimum daily trading volume threshold. In December 2025, the Company satisfied the conditions necessary to call these warrants and exercised its call option. As of December 31, 2025, Tranche A Warrants were exercised to purchase 21,904,261 shares of the Company's common stock for total proceeds of \$23.0 million, \$4.1 million of which was not received until January 2026. The remaining unexercised 500 warrants were cancelled on December 30, 2025 upon expiration of the warrant call.

The fair value of the Tranche A Warrants at issuance was \$7.9 million and was recorded as part of the warrant liabilities on the consolidated balance sheets. The Company remeasured the fair value at the end of each reporting period and again upon exercise, with any adjustments being recorded as a component of other income (expense) in the consolidated statements of operations and comprehensive loss.

Tranche A Warrants fair value at issuance was determined using the Monte-Carlo simulation model with the following key assumptions, which was based on significant inputs that are not observable in the market and represented a Level 3 measurement.

	August 7, 2025
Risk-free interest rate	3.7%
Expected term (in years)	2.0
Expected volatility	110%
Expected dividend yield	0%

The following table provides a rollforward of the fair value of the Tranche A Warrants:

(in thousands)	Fair Value
Fair value at issuance date of August 7, 2025	\$ 7,886
Change in fair value	16,421
Exercise of common stock warrants	(24,307)
Balance as of December 31, 2025	<u>\$ —</u>

August 2025 Tranche B Warrants (“Tranche B Warrants”)

Each Tranche B Warrant has an exercise price per share of our common stock equal to \$1.05, subject to certain adjustments. The Tranche B Warrants became exercisable upon receipt of required stockholder approval at the Special Meeting of Stockholders on October 3, 2025. Any unexercised Tranche B Warrants will expire on October 3, 2030, which is the date that is five years from the date that stockholder approval was received.

The fair value of the Tranche B Warrants at issuance was \$11.0 million and was recorded as part of the warrant liabilities on the consolidated balance sheet. The Company remeasures the fair value at the end of each reporting period, with any adjustments being recorded as a component of other income (expense) in the consolidated statements of operations and comprehensive loss.

Tranche B Warrants fair value was determined using the Black-Scholes valuation model with the following key assumptions, which was based on significant inputs that are not observable in the market and represented a Level 3 measurement.

	December 31, 2025	August 7, 2025
Risk-free interest rate	3.7%	3.8%
Expected term (in years)	4.8	5.2
Expected volatility	75%	85%
Expected dividend yield	0%	0%

The following table provides a rollforward of the fair value of the Tranche B Warrants:

(in thousands)	Fair Value
Fair value at issuance date of August 7, 2025	\$ 10,952
Change in fair value	24,510
Exercise of common stock warrants	(358)
Balance as of December 31, 2025	<u>\$ 35,104</u>

9. Commitments and Contingencies

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, 2025 and 2024.

10. Preferred and Common Stock

Preferred Stock

On January 26, 2024, the Company's board of directors approved an Amended and Restated Certificate of Incorporation, authorizing the Company to issue 10,000,000 shares of undesignated preferred stock at \$0.00001 par value per share. There were no shares of such preferred stock outstanding as of December 31, 2025.

Common Stock

On January 26, 2024, the Company's board of directors approved an Amended and Restated Certificate of Incorporation, authorizing the Company to issue 300,000,000 shares of common stock at \$0.00001 par value per share.

The voting, dividend and liquidation rights of the holders of shares of common stock are subject to and qualified by the rights, powers and preferences of the holders of shares of the Company's undesignated preferred stock, if and when such shares are issued. 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. No dividends have been declared to date. Subject to the rights and preferences of any holders of any shares of any outstanding series of Preferred Stock, in the event of any liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, the funds and assets of the Company that may be legally distributed to the Company's stockholders shall be distributed among the holders of the then outstanding Common Stock pro rata in accordance with the number of shares of Common Stock held by each such holder.

In November 2025, the Company entered into exchange agreements with certain investors pursuant to which these investors exchanged 4,850,000 shares of the Company's common stock for an equal number of pre-funded warrants with an exercise price of \$0.00001 per share. The Company determined that the pre-funded warrants met the requirements for equity classification under ASC 815-40. The Company derecognized the common shares and recognized an equivalent value in pre-funded warrants. In January 2026, these investors exercised all 4,850,000 shares of pre-funded warrants and 4,843,179 shares of common stock were issued as a result of the cashless exercises.

See Note 1—"Nature of the Business" for more details of the Company's recent equity financing activities.

Shares of common stock reserved for future issuance, on an as-if-converted basis, as of December 31, 2025 and 2024, consists of the following:

	December 31,	
	2025	2024
Stock options, issued and outstanding	19,507,294	10,325,811
Unvested RSUs	—	22,500
Stock awards, authorized for future issuance	3,035,013	2,275,046
ESPP, authorized for future issuance	974,624	487,070
Pre-funded warrants	4,850,000	—
Common stock warrants	21,308,618	161,616
Total	49,675,549	13,272,043

The table presented above does not include the number of shares that may be issued upon exercises of the common stock or preferred stock warrants issued in connection with the 2022 Convertible Notes and the 2023 Notes because the number of shares to be issued under these warrants are variable based on a variable exercise price at the warrant holders' option.

11. Stock-Based Compensation

2011 Stock Incentive Plan

The Company's 2011 Stock Incentive Plan, as amended, (the "2011 Plan") provided for the Company to grant restricted stock, restricted stock units, incentive stock options and nonqualified stock options with respect to shares of common stock

to employees, officers, directors, consultants and advisors of the Company. Incentive stock options could only be granted to employees. The 2011 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting schedules and other restrictions of awards were determined at the discretion of the board of directors or by a committee of the board of directors if so delegated, except that the exercise price per share of stock options could not be less than 100% of the fair market value of a share of common stock on the date of grant and the term of stock option could not be greater than ten years. Upon the effective date of the 2024 Incentive Award Plan, as discussed below, the Company ceased granting equity awards under the 2011 Plan.

2024 Incentive Award Plan

On January 26, 2024, the Company's board of directors adopted the 2024 Incentive Award Plan (the "2024 Plan"), which became effective on February 1, 2024. The 2024 Plan provides for the grant of restricted stock, restricted stock units, incentive stock options, nonqualified stock options, stock appreciation rights and other stock or cash-based awards with respect to shares of common stock to employees, officers, directors, consultants and advisors of the Company. The 2024 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting schedules and other restrictions on awards are determined at the discretion of the board of directors or by a committee of the board of directors if so delegated, except that the term of any stock option may not be greater than ten years. The number of shares of the Company's common stock initially reserved for issuance under the 2024 Plan was 4,298,825 shares plus the number of shares subject to awards outstanding under the 2011 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company on or after the effective date of the 2024 Plan. In addition, the number of shares of common stock available for issuance under the 2024 Plan is subject to an annual increase on the first day of each calendar year beginning on January 1, 2025 and ending on and including January 1, 2034 equal to the lesser of (i) 5% of the aggregate number of shares of Common Stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of Common Stock as determined by the Board.

In December 2025, upon the recommendation of the Compensation Committee, the Company's board of directors approved accelerating the annual increase that would otherwise have become effective on January 1, 2026. Accordingly, in December 2025, the number of shares of common stock available for issuance under the 2024 Plan was increased by 7,668,601. As of December 31, 2025, there were 3,035,013 shares available for future grant under the 2024 Plan.

2024 Employee Stock Purchase Plan

On January 26, 2024, the Company's board of directors adopted the 2024 Employee Stock Purchase Plan (the "2024 ESPP Plan"), which became effective on February 1, 2024. The number of shares of the Company's common stock initially reserved for issuance under the 2024 ESPP Plan was 487,070 shares, which is eligible for an annual increase on the first day of each calendar year beginning on January 1, 2025 and ending on and including January 1, 2034 equal to the lesser of (i) 1% of the shares of Common Stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of Common Stock as determined by the Company's board of directors. As of December 31, 2025, there were 974,624 shares available for future issuance under the 2024 ESPP Plan. On January 1, 2026, the number of shares reserved for issuance under the 2024 ESPP Plan increased by 1,533,720 shares. The Company did not issue any shares under the 2024 ESPP Plan during the year ended December 31, 2025.

Stock Options

Stock options granted by the Company generally vest over four years, with some stock option grants vesting as to 25% of the underlying shares after one year and the balance vesting pro rata each month over the following three years and other stock option grants vesting pro rata each month over four years.

In February 2024, the Company granted to certain members of its senior leadership performance-based stock options to purchase a total of 1,157,600 shares of common stock (the "2024 Performance Awards"), with the number of shares eligible to vest determined based on the achievement of certain operational metrics over the period from the grant date through December 31, 2024 (the "performance period"). Any portion of the option for which the applicable milestone is achieved will vest in four substantially equal installments occurring on the final day of the performance period and each of the first three anniversaries thereof. The options have an exercise price equal to the fair market value of the Company's common stock on the grant date and a contractual term of ten years. Final achievement of the "2024 Performance Awards" was determined and approved by the Company's board of directors in January 2025.

In December 2025, the Company granted to certain members of its senior leadership performance-based stock options to purchase a total of 3,250,000 shares of common stock at target performance (up to a maximum of 115% of target), with the number of shares eligible to vest determined based on the achievement of certain operational metrics over the period from the grant date through December 31, 2026. Subject to certification of performance by the Company's board of directors, one-third of any earned shares will vest on the certification date, with the remaining shares vesting in two equal annual installments thereafter, in each case subject to continued service. The options have an exercise price equal to the fair market value of the Company's common stock on the grant date and a contractual term of ten years.

The Company uses the Black-Scholes option-pricing model to estimate the fair value of stock options awards and determine the related compensation expense. The assumptions that the Company used to determine the fair value of stock options granted to employees and directors were as follows:

	Year Ended December 31,	
	2025	2024
Risk-free interest rate	3.7% - 4.3%	3.5% - 4.3%
Weighted average expected term (in years)	6.0	6.1
Weighted average expected volatility	61%	61%
Weighted average expected dividend yield	—%	—%
Fair value of common stock per share	\$1.24	\$6.20

The following table summarizes the Company's stock option activity from December 31, 2024 to December 31, 2025:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2024	10,325,811	\$ 6.75	6.0	\$ 87
Granted	12,248,856	2.08		
Exercised	(164,936)	1.70		
Forfeited/Cancelled	(1,686,444)	8.54		
Expired	(1,215,993)	3.34		
Outstanding at December 31, 2025	19,507,294	\$ 3.92	7.9	\$ 1,631
Options exercisable at December 31, 2025	6,663,156	\$ 5.98	4.4	\$ 256

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2025 and 2024 was \$1.24 and \$6.20 per share, respectively. The total grant date fair value of stock options vested during the years ended December 31, 2025 and 2024 was \$9.0 million and \$5.1 million respectively.

The 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 intrinsic value of stock options exercised during the year ended December 31, 2025 was less than \$0.1 million. The total intrinsic value of stock options exercised during the year ended December 31, 2024 was \$1.4 million.

Restricted Stock Units ("RSUs")

The following table summarizes the Company's RSU activity from December 31, 2024 to December 31, 2025:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2024	22,500	\$ 2.30
Granted	—	—
Vested	(22,500)	2.30
Outstanding at December 31, 2025	—	\$ —

Restricted stock units granted generally have a one-year cliff vesting. Total grant date fair value of RSUs that vested during the year ended December 31, 2025 was \$0.1 million. There were no RSUs outstanding as of December 31, 2025.

Stock-Based Compensation Expense

The Company recorded stock-based compensation expense related to stock options and RSUs in the following expense categories within its consolidated statements of operations and comprehensive loss:

(in thousands)	Year Ended December 31,	
	2025	2024
Research and development expenses	3,040	\$ 6,667
Selling, general and administrative	3,644	7,759
	\$ 6,684	\$ 14,426

As of December 31, 2025, total unrecognized stock-based compensation expense for stock options was \$19.1 million, which is expected to be recognized over a weighted average period of 2.5 years.

12. Income Taxes

During the years ended December 31, 2025 and 2024, 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. The majority of the Company's losses before income taxes were generated in the U.S.

Effective January 1, 2025, the Company elected to prospectively adopt the guidance in ASU 2023-09. The following table is a reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate in accordance with the guidance in ASU 2023-09:

(in thousands, except percentages)	Year Ended December 31,	
	2025	
Loss before income taxes	\$ (140,954)	
Federal statutory income tax	(29,600)	21.0%
Nontaxable or Nondeductible items		
Change in fair value of warrant liability	8,589	(6.1%)
Stock-based compensation	664	(0.5%)
Other nondeductible items	835	(0.6%)
Tax credits	(3,116)	2.2%
Changes in valuation allowance	22,250	(15.8%)
Other	378	(0.2%)
Effective tax rate	\$ —	—%

The following table is a reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate prior to the adoption of ASU 2023-09:

	Year Ended December 31, 2024
Federal statutory income tax rate	21.0%
State income taxes, net of federal benefit	5.3
Research and development tax credits	5.5
Permanent differences	(0.2)
Change in fair value of convertible notes payable	2.5
Change in fair value of warrant liability	5.5
Non-deductible stock compensation	(2.3)
Non-deductible executive compensation	(2.8)
Return to provision	—
Change in valuation allowance	(34.5)
Effective income tax rate	—%

Net deferred tax assets as of December 31, 2025 and 2024 consisted of the following:

(in thousands)	December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	\$ 99,350	\$ 68,932
Research and development tax credit carryforwards	22,692	18,721
Lease liabilities	8,501	8,962
Stock-based compensation expense	1,221	1,264
Accrued expenses and other	1,582	1,527
Capitalized patent and trademark costs	1,369	1,326
Capitalized research and development	20,421	26,463
Other	210	225
Total deferred tax assets	155,346	127,420
Deferred tax liabilities:		
Right-of-use lease assets	(7,167)	(7,597)
Valuation allowance	(148,179)	(119,823)
Net deferred tax assets	\$ —	\$ —

As of December 31, 2025, the Company had federal net operating loss carryforwards of \$374.1 million, of which \$82.7 million begin to expire in 2030 and \$291.4 million will carryforward indefinitely. In addition, the Company had state net operating loss carryforwards of \$329.5 million which begin to expire at various dates beginning in 2030. As of December 31, 2025, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of \$17.4 million and \$5.3 million, 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, 2025 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, 2025 and 2024. 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, 2025 and 2024 related primarily to the increase in federal and state net operating loss carryforwards and available research and development credits and were as follows:

(in thousands)	Year Ended December 31,	
	2025	2024
Valuation allowance at beginning of year	\$ 119,823	\$ 96,239
Increases recorded to income tax provision	28,356	23,584
Valuation allowance at end of year	<u>\$ 148,179</u>	<u>\$ 119,823</u>

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, 2025.

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 US tax returns are still open under statute from 2021 to the present, however carryforward attributes that were generated prior to January 1, 2021 may still be adjusted upon examination by federal or state tax authorities if they have been or will be utilized in a future period.

13. 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 Company's board of directors. The Company has not made any matching or discretionary contributions to date under the 401(k) savings plan.

14. 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,	
	2025	2024
Outstanding stock options	19,507,294	10,325,811
Outstanding restricted stock units	—	22,500
Common stock warrants	21,308,618	161,616
Total	<u>40,815,912</u>	<u>10,509,927</u>

The table presented above does not include the number of shares that may be issued upon exercises of the common stock or preferred stock warrants issued in connection with the 2022 Convertible Notes and the 2023 Notes because the number of shares to be issued under these warrants are variable based on a variable exercise price at the warrant holders' option. Pre-funded warrants to purchase 4,850,000 shares of common stock were also excluded from the table presented above as they

were considered common stock outstanding for the purpose of earnings per share calculation and therefore were included in the calculation of both basic and diluted net loss per share.

15. Segment Information

For the year ended December 31, 2025, the Company has identified one operating and reportable segment. The Company defines its operating segments based on internally reported financial information that is regularly reviewed by the Chief Operating Decision Maker (“CODM”) to analyze financial performance, make decisions, and allocate resources. The Company’s Chief Executive Officer is the CODM.

The Company’s CODM views specific categories within research and development expenses and selling, general and administrative expenses in total as significant given the direct correlation between cash burn and profitability as a pre-commercial company. The following table reconciles reported revenues to net loss under the significant expense principle for the years ended December 31, 2025 and 2024:

(in thousands)	Year Ended December 31,	
	2025	2024
Revenue	\$ —	\$ 93
Less:		
Cost of goods sold	—	50
Research and development:		
Revita direct program expenses	28,892	25,873
Rejuva direct program expenses	11,685	7,220
Indirect expenses	7,965	9,038
Personnel-related expenses	25,994	28,340
Total research and development expenses	74,536	70,471
Selling, general and administrative	22,280	23,103
Other income (expense), net	(44,138)	24,837
Segment net loss	\$ (140,954)	\$ (68,694)

16. Subsequent Events

Change in Chief Financial Officer

On January 6, 2026, the Company announced that Lara Smith Weber was appointed Chief Financial Officer, effective January 12, 2026, succeeding Lisa Davidson, who resigned effective December 31, 2025. In connection with her resignation, Ms. Davidson entered into a transitional consulting agreement with the Company.

In connection with Ms. Smith Weber’s appointment, the Company’s board of directors approved an inducement equity award outside of the Company’s 2024 Incentive Award Plan under Nasdaq Listing Rule 5635(c)(4). The shares underlying this award were registered for issuance on Form S-8 filed with the SEC on January 13, 2026.

Nasdaq Minimum Bid Price Notice

On March 13, 2026, the Company received a letter from Nasdaq Stock Market LLC (“Nasdaq”) notifying the Company that it was not in compliance with the minimum bid price requirement of Nasdaq Listing Rule 5450(a)(1) because the closing bid price of the Company’s common stock had been below \$1.00 per share for 30 consecutive business days. The Company has 180 calendar days, or until September 9, 2026, to regain compliance with the minimum bid price requirement. The notice has no immediate effect on the listing or trading of the Company’s common stock on the Nasdaq Global Market.

Termination of ATM Offering

On March 23, 2026, the Company provided notice to Jefferies LLC of its termination of the Sales Agreement associated with the ATM Offering. As a result, no further sales of the Company’s common stock will be made under the ATM Offering after the termination takes effect on April 6, 2026.

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Management Team

**Harith Rajagopalan,
M.D., Ph.D.**
Co-Founder and Chief
Executive Officer

Jay Caplan
Co-Founder, President and
Chief Product Officer

Lara Smith Weber
Chief Financial Officer
and Treasurer

Sarah Toomey
General Counsel and
Corporate Secretary

Jon Fitzgerald
Senior Vice President of
Regulatory, Quality, and
Clinical

Len Rosberg
Vice President of Manufacturing

Board of Directors

Ajay Royan
Chair of Fractyl Health
Co-Founder and Managing
General Partner, Mithril Capital

Kelly Barnes
Former Partner, PwC

William W. Bradley
Former U.S. Senator

Samuel Conaway
President of Boston Scientific
U.S. Cardiology Sales and
Chair of Close the Gap

Marc Elia
Founder of M28 Capital

**Clive Meanwell,
M.B., Ch.B., M.D.**
Executive Chairman and
Founder of Population
Health Partners

**Harith Rajagopalan,
M.D., Ph.D.**
Co-Founder and Chief
Executive Officer,
Fractyl Health

Ian Sheffield
Managing Partner,
North Country
Holdings, LLC

**Christopher C.
Thompson, M.D., MSc**
Professor of Medicine at
Harvard Medical School and
Director of Endoscopy at
Brigham and Women's Hospital

This letter contains certain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this letter that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding: plans and objectives of management for future operations; the promise and potential impact of our preclinical or clinical trial data and product candidates; the design, initiation, timing and results of clinical enrollment and any clinical studies or readouts; the content, information used for, timing or results of any regulatory developments including Investigational New Drug (IND)-enabling studies, IND applications, Clinical Trial Applications (CTAs), De Novo applications or communications with regulators; the potential launch or commercialization of any of our product candidates or products; the potential treatment population or benefits for any of our product candidates or products; and our strategic and product development objectives and goals, including with respect to enabling long-term control over obesity and type 2 diabetes without the burden of chronic therapies; anticipated cash runway; and the timing of any of the foregoing. Such statements involve known and unknown risks, uncertainties and other important factors that may cause Fractyl Health's actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. For a nonexclusive list of factors which could cause the actual results to differ materially from the forward-looking statements, please refer to the risk factors in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2025, as may be updated from time to time in our quarterly reports on Form 10-Q and other filings with the Securities and Exchange Commission. Any forward-looking statements contained in this letter speak only as of the date hereof, and we specifically disclaim any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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.

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 letter, 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.



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Revita is for investigational use only in the United States under Federal Law.

Revita has a CE mark in the EU/UK.

Rejuva is an investigational preclinical asset and is currently under review for clinical research in the EU and AUS. It has yet to be assessed by the FDA.

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