SEPTERNA, INC.

2025 ANNUAL REPORT TO STOCKHOLDERS

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

FORM 10-K

☒ **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 001-42382

Septerna, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**84-3891440** **(I.R.S. Employer Identification No.)**
250 East Grand Avenue **South San Francisco, CA** **(Address of principal executive offices)**	**94080** **(Zip Code)**

Registrant's telephone number, including area code: (650) 338-3533

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, par value $0.001 per share	SEPN	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer ☐	Accelerated Filer ☐
Non-accelerated Filer ☒	Smaller Reporting Company ☒
	Emerging Growth Company ☒

If an emerging growth company, indicate by 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 ☒

As of June 30, 2025, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $363.3 million, based on the closing price of the registrant's common stock on the Nasdaq Global Market of $10.57 per share as of such date. In determining the market value of non-affiliate common stock, shares of the registrant's common stock beneficially owned by officers, directors and affiliates have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 2, 2026, the registrant had 44,906,374 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2026 Annual Meeting of Stockholders, to be filed with the Securities and Exchange Commission pursuant to Regulation 14A 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 Annual Report on Form 10-K to the extent stated herein.

TABLE OF CONTENTS

We own various U.S. federal trademark filings, including a registered trademark, and possess proprietary trademark rights in our name and logo that we use in connection with the operation of our business. This Annual Report on Form 10-K (this "Annual Report") includes our trademarks and trade names which are protected under applicable intellectual property laws and are our property. This Annual Report 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 may appear without the ®, ™ or SM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent permitted under applicable law, our rights or the right of the 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.

From time to time, we may use our website, our X (formerly known as Twitter) account at Septerna_Inc and our LinkedIn account at https://www.linkedin.com/company/septernainc/ to distribute material information about us and for complying with our disclosure obligations under Regulation FD. Our financial and other material information is routinely posted to and accessible on the Investors section of our website, available at *www.Septerna.com*. Investors are encouraged to review the Investors section of our website because we may post material information on that site that is not otherwise disseminated by us. Information that is contained in and can be accessed through our website or our social media are not incorporated into, and does not form a part of, this Annual Report.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains express or implied forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other 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 these forward-looking statements. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- the initiation, timing, progress, results and costs of conducting our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our current and future programs;
- the potential therapeutic benefits of our product candidates, including our SEP-479 and SEP-631 programs;
- our ability to demonstrate, and the timing of, preclinical proof-of-concept *in vivo* and *ex vivo* for multiple programs;
- our ability to replicate positive results achieved in our preclinical studies or clinical trials in current or future clinical trials;
- our ability to obtain and maintain regulatory approval for our current and future product candidates and research and development programs, including our SEP-479 and SEP-631 programs, and to advance any product candidates that we may identify and successfully complete any clinical studies, including the manufacture of any such product candidates;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of Investigational New Drug ("IND") applications or comparable foreign applications, and final U.S. Food and Drug Administration (the "FDA") approval of our product candidates;
- the timing, scope or likelihood of foreign regulatory filings and approvals;
- the implementation of our business model, and strategic plans for our business, product candidates, and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and other product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- developments relating to our competitors and our industry;
- our ability to leverage programs within our initial target indications and to progress additional programs to further develop our pipeline;
- our ability of our preclinical studies and clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the partnership with Novo Nordisk A/S ("Novo") and the intended and potential benefits thereof, including the receipt of potential milestone payments and royalty payments from commercial product sales, along with tiered royalties based on global net sales, if any;
- Novo's ability to develop and commercialize potential oral small molecule therapies for metabolic-related diseases and the potential of G protein-coupled receptors, including the GLP-1, GIP, and glucagon receptors, to address the unmet medical need for treating obesity, type 2 diabetes and other related conditions;
- our ability to maintain existing collaborations and strategic partnerships, to identify and enter into future license agreements and collaborations, and to realize the intended and potential benefits of such agreements and collaborations;
- our ability to rely on third-party manufacturers and successfully manufacture product candidates for preclinical use, clinical trials and on a larger scale for commercial use, if approved;
- our ability to realize the benefits of collaborations for the development and commercialization of our product candidates;
- our ability to commercialize any of our product candidates;
- developments related to our proprietary Native Complex Platform®;

- regulatory developments in the U.S. and foreign countries;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets;
- our need for and ability to attract and retain key scientific, management and other personnel and to identify, hire, and retain additional qualified professionals;
- our expectations regarding the period during which we will remain an emerging growth company under the Jumpstart Our Business Startups Act of 2012 ("JOBS Act");
- the period over which we expect our existing cash, cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements;
- our anticipated use of our existing resources;
- our financial performance and estimates of our future expenses, capital requirements, and our needs for additional financing;
- the impact of macroeconomic and geopolitical developments (such as the ongoing conflict in Ukraine, and new conflicts in Iran and the Middle East) on our business, including rising inflation and capital market disruptions, changes in or disruptions of U.S. governmental agencies, whether from a future U.S. federal government shutdown or reduced resources, new or increased international tariffs and retaliatory tariffs, trade protection measures, economic sanctions and economic slowdowns or recessions that may result from such developments which could harm our research and development efforts as well as the value of our common stock and our ability to access capital markets; and
- other risks and uncertainties, including those listed under the section titled "Risk Factors" in Part I, Item 1A of this Annual Report.

In some cases, you can identify forward-looking statements by terminology such as "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target," "contemplate," "possible," "can," or the negative of these terms or other comparable terminology, and similar expressions, although not all forward-looking statements contain these identifying words. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled "Risk Factors" and elsewhere in this Annual Report. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report and the documents that we reference in this Annual Report and have filed with the Securities and Exchange Commission (the "SEC") thereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We do not undertake any obligation to publicly update any forward-looking statement except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

This Annual Report also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. All of the market data used in this Annual Report involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

This Annual Report contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed as exhibits to this Annual Report. Unless the context otherwise requires, reference in this Annual Report to the terms "Septerna," the "Company," "we," "us," "our," and similar designations refer to Septerna, Inc.

SUMMARY OF MATERIAL AND OTHER RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties and are subject to change based on various factors, including those highlighted in the section entitled "Risk Factors" and elsewhere in this Annual Report. These risks include, but are not limited to, the following:

- We have a limited operating history and have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future.
- We will require substantial additional funding in order to finance our operations. If we are unable to raise additional capital when needed on acceptable terms, or at all, we may be forced to delay, reduce, or terminate certain of our research and product development programs, future commercialization efforts or other operations.
- We are early in our development efforts. We have not successfully completed any advanced clinical trials, and as a result it will be years before we commercialize a product candidate, if ever. If we are unable to identify and advance product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.
- Preclinical and clinical drug development is a lengthy and expensive process, with uncertain timelines and outcomes. If preclinical studies or clinical trials of our product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our therapeutic candidates or any of our future therapeutic candidates on a timely basis or at all.
- We may encounter substantial delays in the commencement, enrollment or completion of our planned clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing any product candidates we determine to develop on a timely basis, if at all.
- Serious adverse events, undesirable side effects or other unexpected properties of our product candidates may be identified during development or after approval, which could lead to the discontinuation of our clinical development programs, refusal by regulatory authorities to approve our product candidates or, if discovered following marketing approval, revocation of marketing authorizations or limitations on the use of our product candidates, any of which would limit the commercial potential of such product candidate.
- Our product candidates are subject to extensive regulation and compliance obligations, which is costly and time-consuming and which may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.
- Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, which could adversely affect our business, operating results and prospects.
- Our proprietary Native Complex Platform® is based on novel technologies that are unproven and may not result in approvable or marketable products, which exposes us to unforeseen risks and makes it difficult for us to predict the time and cost of product development and potential for regulatory approval, and we may not be successful in our efforts to expand our development portfolio of product candidates.
- We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may invest significant resources to develop these capabilities. If we are unable to establish marketing, sales or distribution capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue.
- Even if any of our product candidates receive marketing approval, such product candidate may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us.
- We rely on third-party manufacturers, clinical research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and suppliers to supply, develop and test components of our product candidates. The loss of our third-party manufacturers, CROs, CMOs, or suppliers, their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, or changes in methods of product candidate manufacturing, development or formulation would materially and adversely affect our business.

The material and other risks summarized above should be read together with the text of the full risk factors and in the other information set forth in this Annual Report, including our financial statements and the related notes, as well as in other documents that we file with the SEC. If any such material and other risks and uncertainties actually occur, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks summarized above or described in full are not the only risks that we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, prospects, financial condition and results of operations.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company pioneering a new era of G protein-coupled receptor ("GPCR") oral small molecule drug discovery powered by our proprietary Native Complex Platform®. Our industrial-scale platform aims to unlock the full potential of GPCR therapies and has led to the discovery and development of our deep pipeline of product candidates focused initially on treating patients in three therapeutic areas: endocrinology, immunology and inflammation, and metabolic diseases.

GPCRs are the largest and most diverse family of cell membrane receptors and regulate physiological processes in nearly every organ system of the human body. Due to their significant role in human diseases, GPCRs have been the most productive target class in drug discovery history, accounting for approximately one-third of all FDA-approved drugs, representing approximately 500 products with combined global revenue of approximately $125 billion in 2023. Despite the pharmacological and commercial success of GPCR-targeted agents, about 75% of potential GPCR therapeutic targets remain undrugged. For certain validated GPCRs, novel binding pockets may exist that could offer enhanced therapeutic benefits. Each step in GPCR activation involves subtle conformational changes that have been historically challenging to reproduce outside of a cell. The inability to isolate GPCR proteins in their native functional form outside of a cellular context has prevented scientists from leveraging some of the state-of-the-art technologies that have revolutionized drug discovery in other major target classes over the past decade. This complex challenge has limited GPCR drug discovery, particularly the development of novel oral small molecules, such as agonists for peptide GPCRs and allosteric modulators.

Our proprietary Native Complex Platform® replicates the natural structure, function, and dynamics of GPCRs outside of cells at an industrial scale for, as we believe it, the first time. Our foundational technologies enable us to isolate, purify, and reconstitute full-length, properly folded GPCR proteins within ternary complexes with ligands and transducer proteins in a lipid bilayer that mimics the cell membrane. We then apply state-of-the-art discovery tools and technologies to these defined and tunable protein complexes to structurally design, screen for, and optimize potential product candidates. Leveraging our platform, we conduct GPCR oral small molecule drug discovery using an industrialized and iterative structure-based drug design approach for a diverse collection of GPCR targets. Our Native Complex Platform® is designed to enable us to target specific GPCRs, uncover novel binding pockets for validated receptors, and pursue a wide spectrum of pharmacologies, including agonists (which activate GPCR signaling), antagonists (which inhibit GPCR signaling), and allosteric modulators (which either increase or decrease the degree of GPCR activation by endogenous ligands) to affect GPCR signaling in different ways to achieve desired therapeutic effects.

We are advancing a deep portfolio of oral small molecule GPCR-targeted programs with novel mechanistic approaches to treat diseases across multiple therapeutic areas for patients with significant unmet needs. Our wholly-owned pipeline is focused initially on three therapeutic areas: endocrinology, immunology and inflammation, and metabolic diseases. We intend to evaluate opportunities in other major therapeutic areas, such as neurology, women's health, cardiovascular, and respiratory disease.

GPCRs as Therapeutic Targets

GPCRs regulate physiological processes in nearly every organ system of the human body and are the most targeted drug class due to their significant role in human diseases and their pharmacological tractability. Nearly one-third of all FDA-approved drugs in the United States, representing approximately 500 products, target GPCR-associated pathways. In fact, GPCR-related drugs comprise approximately 27% of global pharmaceutical sales.

GPCRs are proteins that span the cell membrane seven times, and their primary function is to recognize extracellular substances, or ligands, and transmit signals across the cell membrane to the inside of the cell. Ligand binding induces conformational changes in GPCRs, forming complexes with signal transducers, including G proteins. These transducers interact with second messengers, modulating various cellular processes. Certain GPCR ligands are capable of activating multiple pathways through different transducers, leading to diverse physiological and pathological effects.

GPCRs constitute the largest and most diverse family of cell membrane receptors, with around 800 identified members. GPCRs are key therapeutic targets due to their vital roles in a variety of physiologic processes including immune regulation, nervous system transmission, mood and behavior regulation, sensory transmission, and maintaining cardiovascular and gastrointestinal homeostasis. Despite the pharmacological and commercial success of GPCR-targeted agents, a majority of GPCR therapeutic targets remain undrugged. Each step in GPCR activation involves subtle conformational changes that have been historically challenging to reproduce outside of a cell. The inability to isolate GPCR proteins in their native functional form outside of a cellular context has prevented scientists from leveraging some of the state-of-the-art technologies that have revolutionized drug discovery in other major target classes over the past decade. This complex challenge has limited GPCR drug discovery, particularly the development of novel oral small molecules, such as agonists for peptide GPCRs and allosteric modulators.

To date, drug discovery has been highly concentrated on a small number of GPCRs. More than 70% of current GPCR-related drugs target only six subfamilies of GPCRs. There are about 400 known non-olfactory GPCRs, each represented as a branch on the phylogenetic tree in **Figure 1** below.

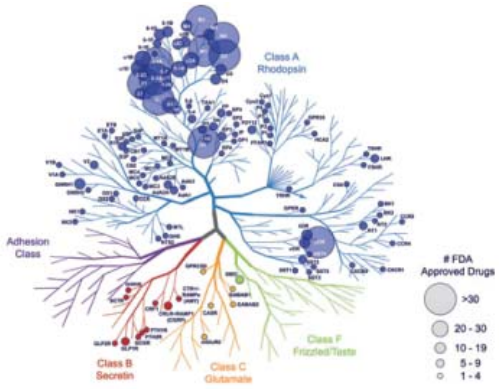


Figure 1. GPCR phylogenetic tree highlighting the number of FDA-approved drugs for each GPCR as of February 2024.

Today, approximately 75% of potential GPCR therapeutic targets remain undrugged, representing significant opportunity to address a vast range of therapeutic areas and diseases. And, even for certain validated GPCRs, novel binding pockets may exist that could offer enhanced therapeutic benefits.

Our Native Complex Platform®

In the past decade, drug discovery across various target classes has been revolutionized by state-of-the-art tools and technologies, including structure-based drug design, computational docking, and DNA-encoded libraries ("DELs"). However, the utilization of these technologies has been limited for discovering oral small molecules targeting GPCRs due to the inability to isolate functional native GPCR proteins outside of a cellular context.

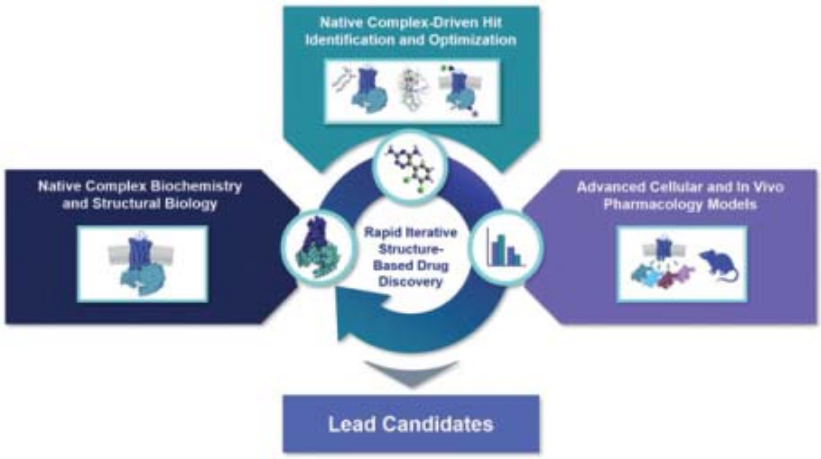
With our proprietary Native Complex Platform®, we can purify GPCRs outside of cells and reconstitute them into fully functional ternary complexes with transducer proteins (e.g., G proteins, beta-arrestins) and ligands (endogenous or synthetic), all housed within a well-defined lipid bilayer environment. These Native Complexes are full-length, properly folded GPCRs that retain their natural structure, function, and dynamics. We then apply state-of-the-art discovery tools and technologies to these defined and tunable protein complexes to structurally design, screen for, and optimize potential product candidates. Leveraging our platform, we are advancing a new approach to GPCR drug discovery, designed to expand the landscape of druggable GPCR targets with novel oral small molecule medicines for patients.

Our Native Complex Platform® is powered by a suite of tools and technologies that we have optimized and integrated into a proprietary and industrialized workflow, forming an efficient and iterative discovery process for identification and optimization of novel small molecule product candidates targeting high-value GPCRs, including:

- ***Native Complex biochemistry and structural biology:*** Our Native Complexes reconstitute native GPCR function in a purified biochemical format, enabling efficient high-resolution, three-dimensional structure determination using cryogenic electron microscopy ("cryo-EM"). This reveals receptor binding pockets that we can target with a range of pharmacologies (e.g., agonists, antagonists, and allosteric modulators) as well as novel insights into mechanisms for GPCR modulation.
- ***Native Complex-driven hit identification and optimization:*** We virtually screen our GPCR structures against ultra-large-scale computational databases containing billions of candidate molecules to identify the most promising small molecule compounds that bind in pockets on the GPCR structure. We use technologies, including DELs, to screen billions of candidate molecules simultaneously and have developed proprietary technologies to discover and optimize compounds with a variety of modes of action. Additionally, we use our proprietary Native Complex biochemical screens in our hit identification and optimization processes.
- ***Advanced cellular and in vivo pharmacology models:*** We efficiently evaluate hits and lead compounds through the integration of advanced cellular and in vivo pharmacology models. Prioritized compounds with desired pharmacologies are

either advanced as potential drug candidates or fed back into the process for additional Native Complex-driven compound optimization.

Our oral small molecule drug discovery process, powered by our proprietary Native Complex Platform®, is depicted in the figure below.



Our industrial-scale Native Complex Platform® is designed to target certain GPCRs for the first time, uncover novel binding pockets for validated receptors, and pursue a wide spectrum of pharmacologies to achieve desired therapeutic effects. Our platform has led to the discovery and development of a pipeline of novel, highly potent and selective oral small molecules, and for our most advanced programs, optimized them into clinical development candidates.

Our Strategy

Our goal is to develop life-changing GPCR-targeted medicines for patients with significant unmet medical needs. We plan to achieve this goal by efficiently advancing our portfolio of GPCR-targeted programs, continuing to expand our differentiated GPCR-targeted pipeline focused on indications with significant unmet needs, maximizing the potential of our Native Complex Platform® through continued innovation and investment, and evaluating potential value-creating strategic partnerships.

Portfolio Opportunities Targeting the Full Breadth of GPCRs

There are significant unmet medical needs across numerous GPCR-driven diseases. Our portfolio is focused initially on three therapeutic areas with the potential to expand to additional therapeutic areas in the future:

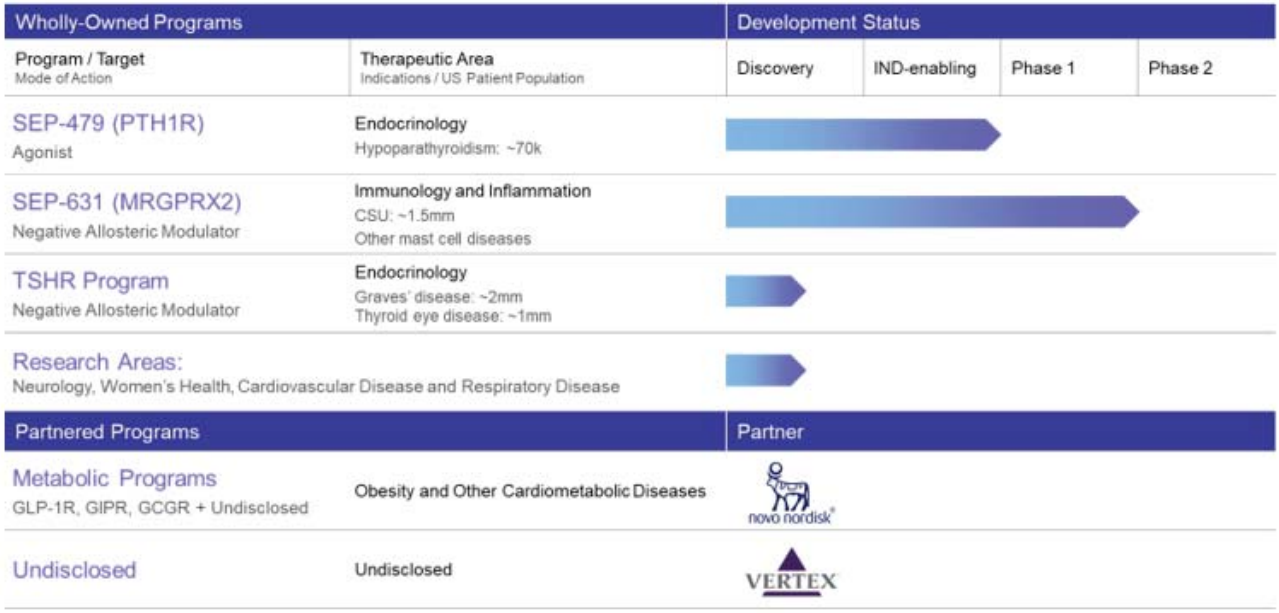
- ***Endocrinology:*** The endocrine system involves glands that secrete hormones into the bloodstream that have effects on other tissues. Central to this system are GPCRs, which serve as primary receptors for many circulating hormones. GPCR biology is at the center of endocrine diseases, such as hypoparathyroidism and Graves' disease, highlighting the urgency for therapeutic interventions targeting GPCR-mediated endocrine disorders. Other endocrine disorders, like osteoporosis, impacts more than 10 million older adults in the United States and could benefit from a small molecule GPCR-directed therapy to help rebuild bone mass.
- ***Immunology & inflammation:*** GPCRs serve as key signaling molecules in various cellular processes, including involvement in the regulation of immune responses and the activation of immune cells such as macrophages, T cells, and dendritic cells. Upon activation by extracellular ligands, GPCRs initiate intracellular signaling cascades that modulate cytokine production, leukocyte trafficking, and inflammatory mediator release. Dysregulation of GPCR signaling pathways is implicated in numerous inflammatory and autoimmune diseases, such as chronic spontaneous urticaria ("CSU"), making them attractive targets for therapeutic intervention.
- ***Metabolic diseases:*** GPCRs are known to regulate various physiological processes such as energy metabolism, glucose homeostasis, and lipid metabolism. These receptors are involved in sensing nutrients, hormones, and other signaling molecules, thereby influencing appetite, insulin secretion, and lipid storage. Dysregulation of GPCR signaling pathways is associated with metabolic disorders, such as obesity and type-2 diabetes ("T2D"). For instance, GPCRs like adrenergic

receptors regulate lipolysis and thermogenesis, while receptors such as the GLP-1 receptor modulate insulin secretion and satiety. Targeting GPCRs is a clinically and commercially validated approach for the development of therapeutics that manage metabolic disorders, offering the potential to manage glucose levels, promote weight loss, and improve metabolic health.

Beyond our initial therapeutic areas of focus, we intend to evaluate opportunities in additional therapeutic areas where GPCRs are directly connected to disease pathology, including in areas of neurology, women's health, cardiovascular disease, and respiratory disease.

Our Pipeline

We are advancing a deep portfolio of highly potent and selective oral small molecule GPCR-targeted programs with novel mechanistic approaches to treat diseases across multiple therapeutic areas for patients with significant unmet needs. Our wholly-owned pipeline is focused initially on three therapeutic areas – endocrinology, immunology and inflammation, and metabolic diseases – and is summarized in the figure below.



Our target selection process considers the validation level of the GPCR and existing preclinical and/or clinical data demonstrating desired biological outcomes upon target modulation for a variety of different indications. We have prioritized indications with well-defined biomarkers to streamline the path to clinical proof-of-concept data, high unmet medical need and significant market opportunities. When analogous molecules exist that are approved or in clinical development, we explore differentiation opportunities and leverage our Native Complex Platform® to address known limitations. We also leverage regulatory insights from established precedents to guide each program's development strategy. As we expand our portfolio of GPCR-targeted programs, we will continue to focus on targets and indications with well-understood biology, predictive biomarkers for early proof-of-concept, efficient clinical development pathways, and high unmet medical need. We are building a deep portfolio comprised of programs that we can independently develop and commercialize upon regulatory approval, alongside select programs that may benefit from the development and commercial expertise, infrastructure and financial support of a strategic partner.

PTH1R Program: Oral Small Molecule PTH1R Agonist for Hypoparathyroidism

We are developing novel, oral small molecule Parathyroid Hormone 1 Receptor ("PTH1R") agonists for the treatment of hypoparathyroidism. While there are PTH peptide products approved and in development for hypoparathyroidism that target PTH1R, to our knowledge, we have the most advanced and comprehensive oral small molecule PTH1R agonist program. We believe our PTH1R agonists offer potent and selective activation of PTH1R, a GPCR highly involved in blood calcium control, with the potential to achieve sustained normalization of serum calcium and phosphate upon once-daily or twice-daily oral dosing.

In the third quarter of 2024, we initiated a Phase 1 single- and multiple-ascending dose ("SAD/MAD") clinical trial of SEP-786 in healthy volunteers. SEP-786 is an oral small molecule PTH1R agonist product candidate that was being developed for the treatment of hypoparathyroidism. On February 18, 2025, we announced our decision to discontinue the development of SEP-786 and advance a next-generation oral small molecule PTH1R agonist. This decision followed the observation of two unanticipated severe (Grade 3) events of elevated unconjugated bilirubin in the MAD portion of the Phase 1 trial, both of which were without elevations in alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase liver enzyme levels. Dosing was discontinued for both study participants, and the bilirubin elevations were reversible. There were no events of liver injury, cholestasis, or hemolysis across all participants, and there were no serious adverse events ("SAEs") in the Phase 1 trial. In completed 28-day preclinical toxicology studies in rats and dogs, SEP-786 was generally well-tolerated, without predicted risk of bilirubin elevation. We observed early signals of on-target pharmacology in the MAD portion of the trial including initial increases in serum calcium and decreases in endogenous parathyroid hormone levels. In September 2025, we announced the findings from our post-discontinuation investigation that SEP-786 was a potent UGT1A1 inhibitor, which is a mechanism known to be associated with increases in unconjugated bilirubin. In a follow-up cynomolgus monkey study of SEP-786, conducted after clinical discontinuation, we also observed elevated unconjugated bilirubin levels.

We announced in September 2025 that we had selected a new PTH1R development candidate, SEP-479. We presented preclinical data for SEP-479 from a translational rat thyroparathyroidectomy model demonstrating that SEP-479 achieved sustained normalization of serum calcium and phosphate levels over a 28-day dosing period. We also conducted a seven-day pharmacokinetic ("PK") / pharmacodynamic ("PD") study of SEP-479 in healthy cynomolgus monkeys, which showed robust, dose-dependent increases in serum calcium and decreases in endogenous parathyroid hormone levels across multiple dose levels of SEP-479. We observed no significant inhibition of UGT1A1 or other transporters for SEP-479 and no hyperbilirubinemia in any of the non-clinical studies to date for SEP-479, including the 7-day and 28-day GLP toxicology studies in healthy cynomolgus monkeys. SEP-479 was generally well-tolerated in 28-day GLP toxicology studies in rats, dogs and cynomolgus monkeys. In the first half of 2026, we plan to initiate a placebo-controlled, SAD and MAD Phase 1 clinical trial in Australia, pending the successful completion of regulatory submissions. We anticipate announcing topline data from this Phase 1 clinical trial around the end of 2026 or early 2027.

Overview of Hypoparathyroidism

Disease Background and Role of PTH1R

Hypoparathyroidism is a rare endocrine disease characterized by insufficient levels of parathyroid hormone ("PTH") that affects approximately 70,000 patients in the United States and 140,000 patients in Europe. PTH is a critical hormone for calcium and phosphate homeostasis and functions through activation of PTH1R. Under normal physiological conditions, PTH is released from the parathyroid glands when circulating calcium levels are reduced and will act on PTH1R expressed on bone and kidney cells to increase calcium levels. Most patients with hypoparathyroidism develop the condition following damage to or loss of the parathyroid glands during thyroid surgery, while other etiologies include autoimmune and genetic disorders. Patients with hypoparathyroidism are at risk of both short-term and long-term complications and comorbidities, such as tingling, muscle cramps and weakness, fatigue, cataracts, and in severe cases can lead to life-threatening complications including abnormal heart rhythms and seizures. Chronic hypoparathyroidism is associated with cognitive and emotional symptoms, such as mental lethargy, inability to concentrate, memory loss or forgetfulness, anxiety, and depression. Many patients experience persistent symptoms that negatively impact quality of life and reduce work productivity.

Current Treatment Options and Their Limitations

The standard treatment for hypoparathyroidism includes high-dose calcium supplements several times a day and activated vitamin D (calcitriol) which aim to correct serum calcium levels; however, these therapies do not replace other functions of PTH to restore physiological mineral homeostasis, and they can lead to long-term complications, including soft-tissue calcifications and impaired renal function. Hormone replacement therapy with injectable PTH peptides is designed to sustain PTH in the normal physiological range, thereby more fully addressing the underlying condition. An injectable PTH peptide, palopegteriparatide (marketed as Yorvipath by Ascendis Pharma), was approved in Europe in 2023 and in the United States in 2024; however, it will require life-long daily injections.

Our Solution: Oral Small Molecule PTH1R Agonist

Our Program Strategy

We believe there is an unmet need for an oral small molecule PTH1R agonist that offers hypoparathyroidism patients a convenient, more physiological treatment option. Since conventional therapies, such as calcium and vitamin D, have limitations and do not restore other actions of PTH, such as release of bone calcium or renal calcium reabsorption, we believe an oral option that can increase serum calcium and replace the other functions of PTH is needed for patients. Our potent and selective PTH1R agonists are designed to address all patients with hypoparathyroidism. This includes the most severe patients, who may start injectable PTH peptide therapy, as well as

mild-to-moderate patients who are currently on high doses of calcium and vitamin D and may be less interested in an injectable PTH peptide treatment.

Additionally, our Native Complex Platform® affords us the opportunity to continuously discover and optimize oral small molecule PTH1R agonists in addition to the lead compounds we have already identified. We may develop additional molecules for hypoparathyroidism or for other indications where PTH1R agonists can address disease pathology, such as osteoporosis.

Discovery and Preclinical Activity of Small Molecule PTH1R Agonists

Our Native Complex Platform® was applied to PTH1R and yielded multiple tractable chemical series of small molecule PTH1R agonists with distinct binding sites. Iterative structure-based design has led to multiple lead compounds from different chemical series. In September 2025, we announced that we had selected SEP-479 as the lead compound that we plan to advance into clinical development in the first half of 2026, pending the successful completion of drug product manufacturing and regulatory submissions. SEP-479 was generated from a chemical series that is unrelated to the chemical series from which we generated SEP-786.

We have assessed SEP-479's potency and selective activation of PTH1R in human, dog, and rat receptor cell-based assays. In vivo, we have demonstrated that SEP-479 showed activity in a translational rat thyroparathyroidectomy ("TPTx") model of hypoparathyroidism (**Figure 2.A**). In this model, surgical removal of the parathyroid glands replicates the human disease of hypoparathyroidism with a reduction in serum calcium below the normal range and an increase in serum phosphate levels above the normal range. To assess the activity of SEP-479, we dosed the TPTx rats with SEP-479 once-daily and analyzed the dose-dependent increases in serum calcium and decreases in serum phosphate allowing for an assessment of compound activity and PK/PD relationships.

In a 28-day repeat dose study (**Figure 2.B and C**), SEP-479 was dosed at 0.15 mg/kg orally once-daily which led to sustained increases in serum calcium to within the normal range and normalized serum phosphate levels over the entire 28-day dosing period.

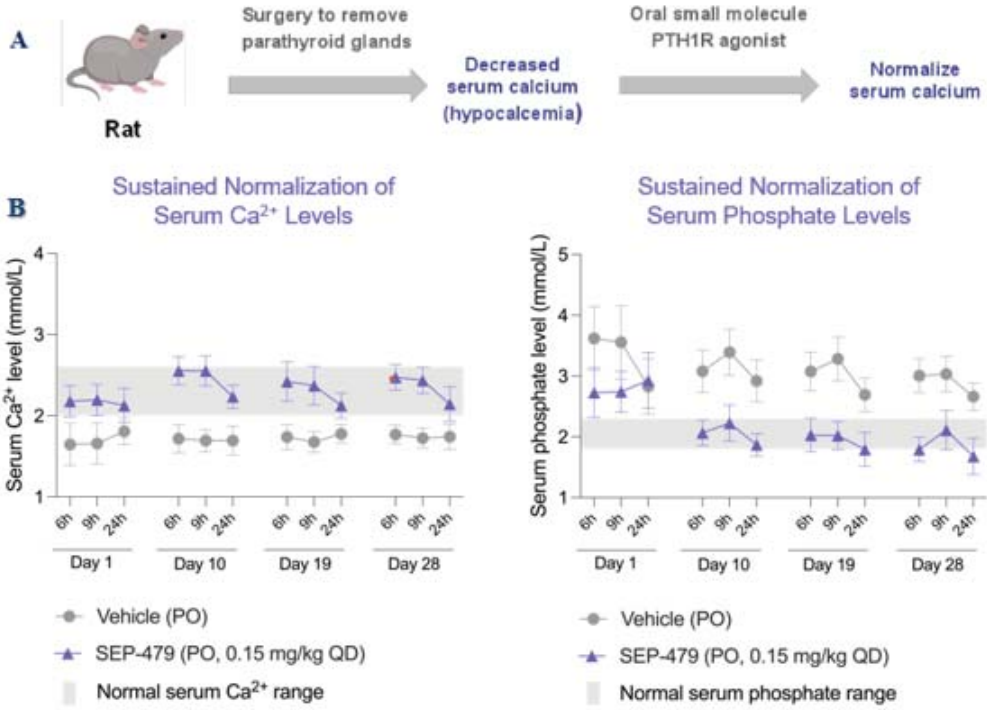


Figure 2. (A) Rat hypoparathyroidism disease model (thyroid-parathyroidectomy model, TPTx). (B) Repeat once-daily oral dosing of SEP-479 in the TPTx model showed sustained calcium and phosphate control over 28 days of dosing. PO = oral; QD = once-daily.

In a 7-day repeat-dose healthy cynomolgus monkey PD study (**Figure 3**), SEP-479 was dosed orally once-daily at 0.5 mg/kg, 1 mg/kg, 2 mg/kg, and 3 mg/kg which led to decreases in serum PTH levels and dose-dependence increases in serum calcium.

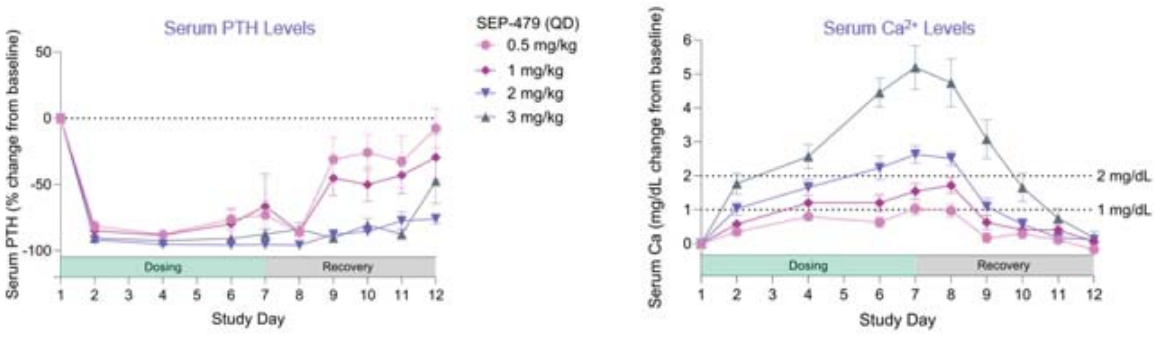


Figure 3. Preclinical pharmacodynamic study of multiple doses of SEP-479 in healthy cynomolgus monkey. (QD) = QD = once-daily.

The PK profile of SEP-479 across multiple species was determined to support human PK projections based upon allometric scaling of the nonclinical PK parameters, in addition to in vitro-in vivo extrapolation (IVIVE) of intrinsic clearance in human hepatocytes. These human PK models projected that SEP-479 will have a human half-life in approximately the range of 43-87 hours following oral dosing. We believe that the totality of preclinical data for SEP-479 supports a projection that once-daily oral dosing of SEP-479 could lead to control of serum calcium within the normal range in patients with hypoparathyroidism.

Clinical Development Plan and Status

In the first half of 2026, we plan to initiate a placebo-controlled, SAD and MAD Phase 1 clinical trial in Australia, pending the successful completion of regulatory submissions. This Phase 1 clinical trial in healthy adult participants is designed to assess preliminary safety, tolerability, PK, and PD of oral doses of SEP-479. In the MAD portion of the trial, we plan to evaluate oral dosing of SEP-479 to evaluate safety and determine the optimal dosing regimen for serum calcium control. Secondary endpoints include PK, serum calcium, serum PTH, and other biomarkers. We anticipate announcing topline data from this Phase 1 clinical trial around the end of 2026 or early 2027.

SEP-631: Oral Small Molecule MRGPRX2 NAM for CSU and Other Mast Cell- Driven Diseases

We are developing SEP-631, a selective, oral small molecule MRGPRX2 negative allosteric modulator ("NAM"), initially for the treatment of CSU. In preclinical studies, SEP-631 demonstrated potent and long-lasting inhibition of MRGPRX2, which is a highly and uniquely expressed receptor on mast cells and when activated is a key driver of CSU and other prevalent mast cell- driven diseases. In August 2025, we announced the dosing of the first participants in our Phase 1 clinical trial of SEP-631. The Phase 1 SAD and MAD clinical trial evaluated the safety, tolerability, PK and PD of SEP-631 in healthy adult volunteers. On March 1, 2026, we presented positive results from our Phase 1 clinical trial of SEP-631 at the 2026 American Academy of Allergy Asthma & Immunology (AAAAI) Annual Meeting.

Overview of CSU

Disease Background and Role of MRGPRX2

CSU is a systemic inflammatory skin disease characterized by the spontaneous and recurrent appearance of itchy, painful hives, known as wheals, on the skin and angioedema, or swelling, that affects approximately 2-3 million patients in the United States. These chronic symptoms, which typically last between two and five years, can interfere with daily living, including the ability to work, and are frequently associated with psychiatric comorbidities, including depression and anxiety. Some patients with CSU report associated systemic symptoms including headache and fatigue, wheezing, flushing, palpitations, and gastrointestinal symptoms.

While there is no known trigger, the activation and degranulation of mast cells and release of histamine and other inflammatory mediators lead to the debilitating symptoms of CSU. Two canonical pathways represent the primary mechanisms for activation and degranulation of mast cells: activation of the IgE pathway via receptor cross-linking by antibodies targeting the high-affinity IgE receptor

(FcεRI) or IgE itself, and activation of an IgE-independent pathway via MRGPRX2. Upon activation, mast cells release a plethora of mediators leading to the hallmark symptoms of itching, redness, and swelling.

MRGPRX2 is highly expressed on the surface of mast cells and plays a critical role in mast cell activation and degranulation. This receptor is activated by a variety of stimuli, including neuropeptides, antimicrobial peptides, immune mediators, and certain drugs. Upon activation, MRGPRX2 triggers a signaling cascade that leads to the rapid release of pre-stored inflammatory mediators such as histamine, proteases, and cytokines from mast cell granules. This degranulation process contributes to immediate hypersensitivity reactions and various inflammatory conditions. The unique ability of MRGPRX2 to respond to a broad range of ligands highlights its importance in host defense mechanisms and its potential as a therapeutic target for treating allergic and inflammatory diseases.

Current Treatment Options and Their Limitations

Patients suffering from CSU are treated initially with antihistamines to control symptoms; however, approximately 37% of patients are inadequately controlled in this first-line setting.

A significant proportion of patients have persistent symptoms with antihistamines, highlighting substantial need for additional treatment options. In 2025, the FDA approved two new treatment options for CSU patients: dupilumab, an injectable biologic that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13), and remibrutinib, a twice-daily oral Bruton's tyrosine kinase inhibitor. With the expanding knowledge of the pathogenesis of CSU and the role of mast cells, novel therapeutic agents targeting distinct drivers of CSU are in development. We are aware of several new mechanisms, and programs are being explored in clinical trials, such as anti-KIT antibodies barzolvolimab and briquilimab, an oral KIT inhibitor SAR449028, an MRGPRX2 inhibitor EVO756, and a long-acting anti-IgE antibody, ozureprubart.

Our Solution: Oral Small Molecule MRGPRX2 NAM

Our Program Strategy

We believe an oral small molecule that targets MRGPRX2 could provide a differentiated treatment option for patients with CSU. Our MRGPRX2 NAM program is designed to selectively inhibit mast cells, minimizing the risk of broad immunosuppression, which might be observed with other mechanistic approaches that either eradicate mast cells or inhibit multiple immune cell types. We believe selective mast cell inhibitors have the potential to be safer treatment alternatives and could be used for both monotherapy and combination therapy. With our NAM, we believe that we may be able to universally block all endogenous MRGPRX2 agonists and prevent MRGPRX2 activation even in the presence of high concentrations of MRGPRX2 agonists. We believe that with this combination of features, our NAM could have the potential to control patient symptoms and protect against disease flares.

We are developing SEP-631 initially for the treatment of CSU, as we believe this may provide an efficient path to clinical proof-of-concept. There remains a significant unmet need in CSU, since antihistamine-refractory patients have few oral treatment alternatives. Because multiple diseases are driven by activated mast cells, we believe there is an opportunity to expand into indications across several therapeutic areas, such as atopic dermatitis, interstitial cystitis, migraine, prurigo nodularis, and asthma.

Preclinical Activity of SEP-631

SEP-631 has been demonstrated to potently block the activation of intracellular signaling in HEK293 cells with overexpressed human MRGPRX2 stimulated by cortistatin-14 (IC50 = 1.6 nM). Experiments using a matrix of different concentrations of SEP-631 versus different concentrations of cortistatin-14 showed strong suppression of maximal agonist effects (**Figure 4**), which we believe demonstrates SEP-631 has the potential to be a NAM which, when bound to MRGPRX2, cannot be outcompeted by excess amounts of an MRGPRX2 agonist.

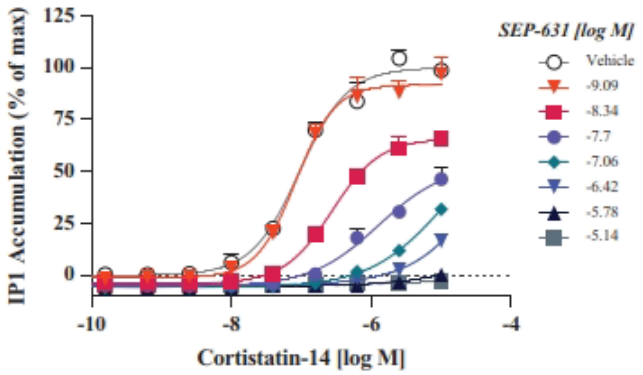


Figure 4. SEP-631 shows strong negative allosteric modulation of cortistatin-14 activation of MRGPRX2 in HEK293 cells expressing MRGPRX2.

SEP-631 can block IP1 accumulation in HEK293 cells expressing MRGPRX2 in response to activation by several clinically relevant endogenous MRGPRX2 agonists (**Figure 5**), demonstrating that its inhibitory effect is independent of the activating agonist (i.e., the inhibitor does not show probe dependence).

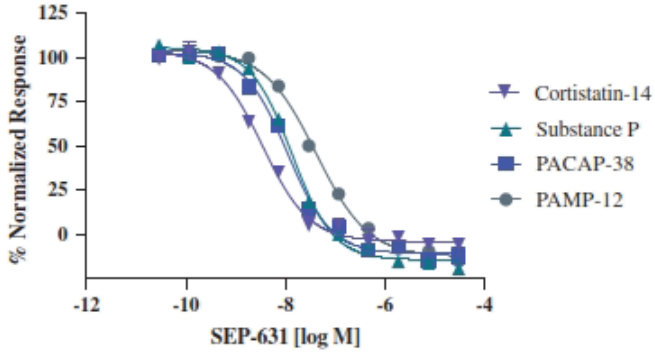


Figure 5. SEP-631 potently inhibits the activation of MRGPRX2 by a range of endogenous MRGPRX2 agonists.

In different in vitro cellular models of mast cell degranulation, SEP-631 was shown to be a potent inhibitor of activation and degranulation in LAD2 cells (IC50 = 2.3 nM) and primary human cord blood-derived mast cells (IC50 = 0.72 nM). In typical experiments on primary human skin mast cells, SEP-631 fully and potently inhibited tryptase release triggered by an EC90 concentration of Substance P (IC50 = 12 nM) (**Figure 6**).

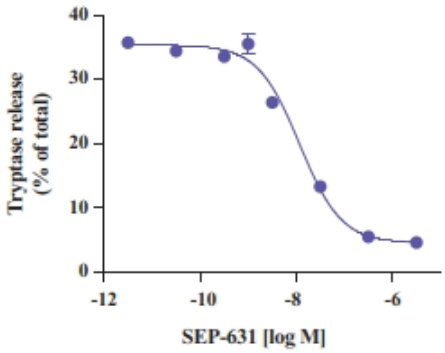


Figure 6. In typical experiments on human skin mast cells, SEP-631 potently inhibited Substance P- stimulated tryptase release from primary human skin mast cells.

A key feature of SEP-631 compared to other MRGPRX2 inhibitors is its long target residence time or slow off-rate of inhibition, meaning it takes a long time for the receptor-ligand complex to dissociate and for the receptor to become activatable again. Two experimental approaches were taken to determine the half-life of the receptor-ligand complex: radioligand binding experiments and a surface plasmon resonance study demonstrated long half-lives of 124 minutes (with a standard deviation of 20 minutes) and 50 minutes, respectively. Long target residence times of receptor ligands are recognized as being potentially advantageous for prolonged drug action in vivo, which have been shown to translate to enhanced clinical activity.

For characterization of SEP-631 in vivo, we developed a transgenic knock-in ("KI") mouse model in which the coding region of the endogenous mouse MRGPRB2 receptor was replaced with the human MRGPRX2 receptor, due to the low sequence homology shared between the mouse and human orthologs. In this model, MRGPRX2 agonist ligands such as cortistatin-14 or icatibant stimulate robust plasma extravasation, or edema, when injected into the skin. Extravasation can be quantitated by following the redistribution of Evans Blue dye from the circulation into skin tissue (**Figure 7.A**). In the MRGPRX2 KI mouse model, SEP-631 robustly inhibited skin extravasation when dosed orally prior to the cortistatin-14 and icatibant skin challenge, demonstrating complete blockade of skin mast cell degranulation at an oral dose of 3 mg/kg (**Figure 7.B**).

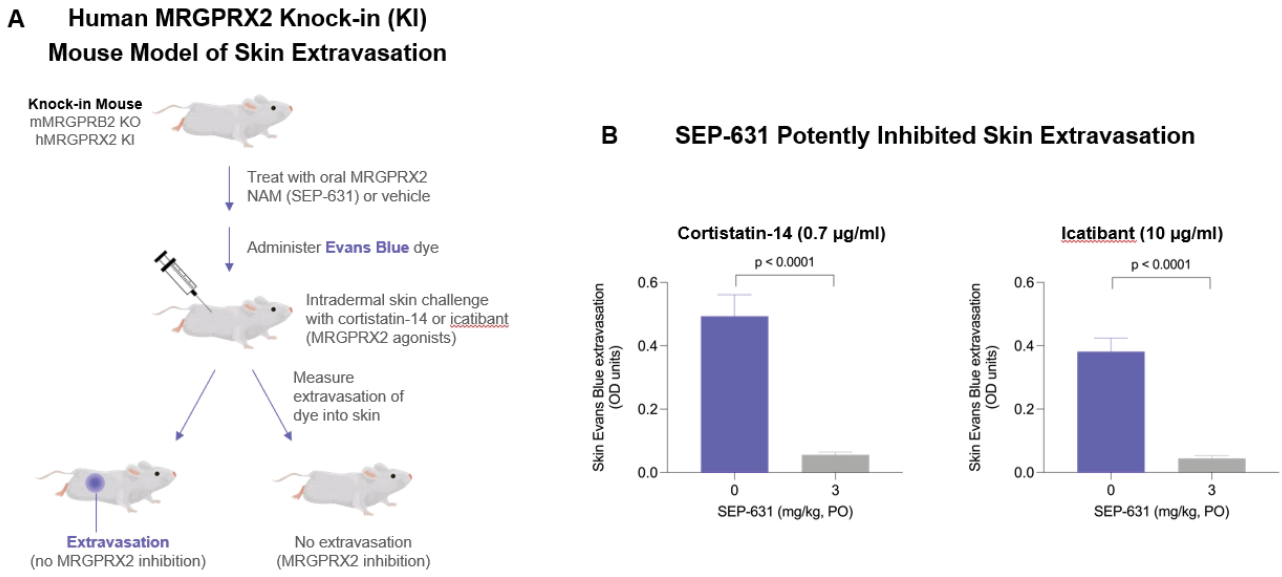


Figure 7. (A) Human MRGPRX2 KI mouse model of plasma extravasation into skin. (B) SEP-631 potently inhibited cortistatin-14 and icatibant mediated plasma extravasation into skin in a human MRGPRX2 KI mouse model. PO = oral.

Preclinical Studies to Support Clinical Advancement of SEP-631

The preclinical drug metabolism and PK profile of SEP-631 across multiple species was determined to support human PK projections. SEP-631 has the potential to be highly orally bioavailable with low clearance and a projected half-life consistent with once-daily oral dosing.

In vitro and in vivo safety studies explored to date support that SEP-631 has a favorable tolerability profile. In 28-day repeat oral dose GLP toxicology studies in rats and dogs, SEP-631 was generally well tolerated with wide safety margins over projected maximal exposures at human efficacious doses.

Phase 1 Study Supports Clinical Advancement of SEP-631 to Phase 2

In August 2025, we announced the dosing of the first participants in our Phase 1 clinical trial of SEP-631. The Phase 1, double-blind, randomized, placebo-controlled, SAD and MAD clinical trial evaluated the safety, tolerability, PK, PD and food effects of SEP-631 dosed orally once-daily ("QD") in healthy adult volunteers. On March 1, 2026, we presented positive results from our Phase 1 clinical trial of SEP-631 at the AAAAI Annual Meeting. In the SAD and MAD cohorts the adverse event profile for SEP-631 was comparable to placebo. No severe or serious events were reported in the study. In the SAD cohorts, two adverse events of mild transaminase elevations (<1.5x the upper limit of normal) in subjects receiving SEP-631, both of which were not related to dose, and at

rates similar to placebo with one mild transaminase elevation observed in a subject receiving placebo. In the MAD cohorts, one mild transaminase elevation (<1.5x the upper limit of normal) was observed in a subject receiving SEP-631 and one was observed with a subject receiving placebo. The observed elimination half-life of SEP-631 was approximately 24 hours which we believe will support QD dosing in future clinical studies of SEP-631. In a food effects evaluation cohort, we observed subjects on a high-fat, high-calorie meal resulted in similar exposure of SEP-631 to subjects in fasted conditions as assessed by the maximum plasma concentration and area under the curve.

The Phase 1 study included a PD assessment of SEP-631 in the MAD cohorts using an icatibant skin challenge. The skin challenge agents that were injected into the forearm of healthy adult subjects included saline (injection negative control), histamine (wheal positive control), and icatibant at 10 ug/mL and 100ug/mL. Icatibant is an MRGPRX2 agonist that is known to cause wheal formations on the skin at the injection site. The skin challenge was performed at baseline (Day –1) and at steady-state (Day 9) following once-daily dosing of SEP-631 or placebo. The size of the wheals in the skin challenge was assessed using a precision image-based technology called AllergyScope detector, which utilizes short-wave infrared spectrum to image the skin wheals. Those images were then transmitted for central lab analysis and adjudication performed by two independent and blinded adjudicators at Johns Hopkins University. SEP-631 substantially inhibited icatibant 10 µg/mL-induced wheals at 10 mg QD, the lowest dose of SEP-631 that was evaluated in the study (**Figure 8.A**). SEP-631 inhibited icatibant 100 µg/mL-induced wheals in a dose-dependent manner up to complete inhibition at 200 mg QD (**Figure 8.B**).

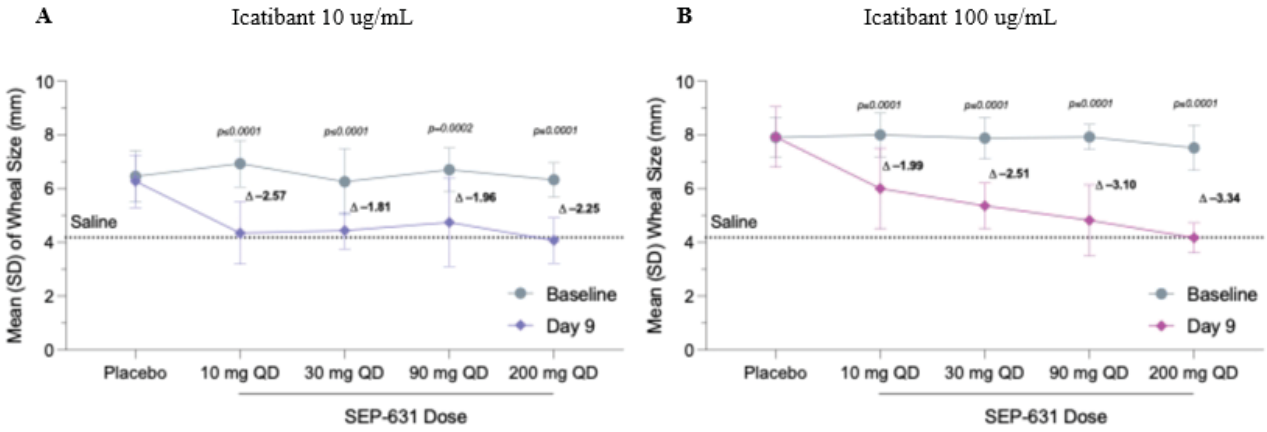


Figure 8. (A) Icatibant 10 ug/mL. (B) Icatibant 100 ug/mL. Note that nominal p-values comparing each SEP-631 dose level to placebo for change from baseline are based on an ANCOVA model including a fixed effect for treatment group and baseline wheal response as a covariate.

Clinical Development Plan and Status

We are currently conducting long-term GLP toxicology studies for SEP-631 in rats and dogs which we expect to be completed summer 2026. Subject to successful completion of these toxicology studies, we plan to initiate a Phase 2b global, randomized, double-blind, placebo-controlled study to evaluate safety and exploratory efficacy of SEP-631 in CSU in the second half of 2026. In addition to CSU, we are exploring other high potential indications where tissue mast cells express MRGPRX2 including atopic dermatitis, interstitial cystitis / bladder pain syndrome, migraine, and asthma where we believe SEP-631 could offer a novel oral treatment option for these patient populations. We plan to explore these indications as potential future clinical development opportunities.

TSHR Program: Oral Small Molecule TSHR NAM for Graves' Disease and TED

We are developing a novel, oral small molecule TSHR NAM for the treatment of Graves' disease and thyroid eye disease ("TED"). We believe our TSHR NAM could offer a disease-modifying treatment that directly addresses the pathobiology of both diseases by blocking TSHR overactivation caused by patients' autoantibodies. We are advancing several lead compounds towards selection of a development candidate for IND-enabling studies.

Overview of Graves' Disease and TED

Disease Background and Role of TSHR

Graves' disease is one of the most prevalent autoimmune conditions affecting over 2 million patients in the United States and is the leading cause of hyperthyroidism. In Graves' disease, the body produces autoantibodies that bind to and activate TSHR on thyroid cells. These autoantibodies stimulate the thyroid gland to produce excess thyroid hormone, resulting in hyperthyroidism. Thyroid hormones affect many body systems, so symptoms of Graves' disease can be wide-ranging. Common symptoms of Graves' disease include anxiety and irritability, tremors, heat sensitivity, weight loss, rapid or irregular heartbeat, and sleep disturbance. Although Graves' disease may affect anyone, it is more common among women and people younger than age 40.

TED is a related, yet distinct, vision-threatening autoimmune condition that develops in approximately 50% of Graves' disease patients. In TED, autoantibodies bind to and activate TSHR on orbital fibroblasts located behind the eyes, thereby resulting in inflammation, orbital fat expansion, and fibrosis. TED is a progressive disease and early diagnosis and treatment are important to prevent worsening and serious eye damage, including proptosis (eye bulging), strabismus (misalignment of the eyes), and diplopia (blurred or double vision).

Current Treatment Options and Their Limitations

The most common treatments for Graves' disease have remained largely unchanged over the past 70 years and include antithyroid drugs, such as methimazole and propylthiouracil, designed to lower the amount of hormone the thyroid makes or block the effects of thyroid hormone on the body, radioactive iodine therapies that aim to destroy overactive thyroid cells, and thyroidectomy surgery to remove all or part of the thyroid. For many patients, there is a high rate of disease recurrence after treatment with antithyroid drugs, and lifelong hypothyroidism develops after ablation and thyroidectomy. In addition, these treatment options may initially address the underlying symptoms, but they are not disease-modifying and do not stop disease progression.

Current treatments for TED depend on disease severity and are designed to help manage symptoms and slow disease progression. For patients with mild TED, lifestyle changes and over-the-counter remedies, such as artificial tear drops and selenium supplements, may help with dry eye relief. For severe TED, steroids and/or eye surgery, such as orbital decompression, may be considered. Historically, patients have had to live with TED until the inflammation subsides, after which they are often left with permanent and vision-impairing consequences and may require multiple surgeries that do not completely return the patient to their pre-disease state.

Our Solution: Oral Small Molecule TSHR NAM

Our Program Strategy

We believe there is a significant unmet need for a disease-modifying approach that directly addresses the pathobiology of both Graves' disease and TED. Our highly selective, oral small molecule TSHR NAM program is designed to block the activation of TSHR by autoantibodies and could lead to a universal treatment option for all Graves' disease and TED patients. Our NAMs are designed to prevent

the activation of TSHR even in the presence of excess amounts of TSHR activating autoantibodies, thus potentially providing protection for patients with high serum antibody levels and for patients with polyclonal activating antibodies.

With few innovative, non-surgical or ablative treatments, we believe that there is a significant unmet need in Graves' disease. While treatments exist for TED, they are focused on the most severe patients, so an oral small molecule TSHR NAM could provide a new option for all TED patients. Because over-stimulation of TSHR is at the center of Graves' disease and TED, we believe that if we can treat Graves' disease patients early in their disease course with our oral small molecule TSHR NAM, our treatment may be able to prevent the progression to other manifestations of the disease, such as TED or Graves' dermopathy.

Discovery and Preclinical Activity of Oral TSHR NAMs

We have used our Native Complex Platform® to identify multiple tractable chemical series of oral small molecule TSHR NAMs. Molecular pharmacology studies with TSHR NAMs have demonstrated multiple compound series with high potencies and desired drug-like properties. In cells expressing human TSHR, cAMP signaling activated by an autoantibody isolated from a Graves' disease patient was significantly inhibited with several of our lead compounds. In addition, our compounds exhibited high selectivity for inhibition of TSHR over a broad set of other GPCRs.

An effective treatment for both Graves' disease and TED will require broad inhibition of patient autoantibodies, which are typically high affinity and present at high titers during active disease. Furthermore, these autoantibodies may bind to different sites on the large extracellular domain of TSHR. We believe a TSHR NAM can have an optimized pharmacologic profile to fully block the activity of all patient autoantibodies.

To demonstrate that our TSHR NAM can fully inhibit multiple patient autoantibodies, we assessed the activity of one of our small molecule TSHR NAMs (SP-1351) against Graves' disease patient-derived polyclonal sera applied to TED patients' orbital fibroblasts. Fibroblast activation by the sera is measured by quantifying hyaluronic acid production by the cells. SP-1351 was able to inhibit the activity of 10 out of 10 polyclonal sera samples, each from a different Graves' disease patient (**Figure 9**). This result suggests broad inhibitory activity of our TSHR NAMs against the diverse range of polyclonal autoantibodies found in Graves' disease patients.

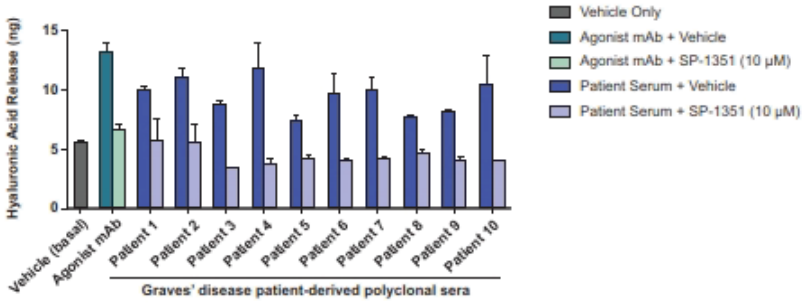


Figure 9. SP-1351 inhibits activation of primary orbital fibroblasts by all 10 polyclonal serum samples collected from Graves' disease patients. mAb = monoclonal antibody.

To characterize the effects of these oral TSHR NAMs on disease manifestations in vivo, we developed a translational mouse model of hyperthyroidism (**Figure 10.A**). Mice chronically treated with a Graves' disease patient-derived TSHR-activating antibody developed multiple manifestations similar to Graves' disease patients, including increased plasma thyroid hormone T4 levels (**Figure 10.B**), increased thyroid weight (**Figure 10.C**), and proptosis (**Figure 10.D**). After one week of SP-1351 treatment with repeat oral dosing, several of these manifestations showed signs of reversal including normalization of thyroid hormone T4 levels, reduction in thyroid weight, and reduction of proptosis.

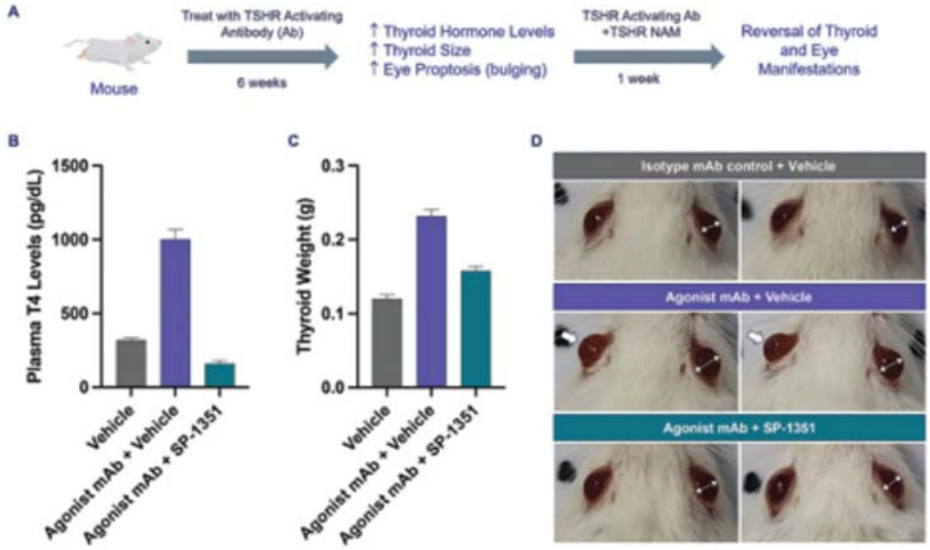


Figure 10. (A) Translational in vivo mouse model of Graves' disease.(B, C, D) SP-1351 demonstrates reversal of the hyperthyroid state and proptosis in mice chronically treated with a monoclonal TSHR autoantibody. mAb = monoclonal antibody.

In the same mouse model, effects on thyroid tissue were assessed. Thyroid glands of Graves' disease patients are characterized by follicular hyperplasia and/or hypertrophy, intracellular colloid droplets, follicular colloid reduction and scalloping, increased vascularity and lymphocyte infiltration, all of which manifest in our mouse disease model. After oral treatment with SP-1351, we observed significant reduction in follicular hypertrophy and colloid droplets.

Next Steps

We are continuing to optimize multiple early-stage oral small molecule TSHR NAMs, with the goal of advancing lead compounds towards selection of a development candidate for IND-enabling studies. In our preclinical studies, we have identified multiple TSHR NAMs that demonstrated the ability to reverse hyperthyroidism and proptosis in a novel mouse model of Graves' disease and inhibit multiple Graves' disease patient TSHR autoantibodies in cell-based assays using primary human cells. We intend to pursue future clinical development of our TSHR NAM program for the treatment of Graves' disease and TED.

Metabolic Diseases: Collaboration with Novo Nordisk

On May 13, 2025, we and Novo Nordisk A/S ("Novo") entered into a global Collaboration and License Agreement (the "Collaboration Agreement"). Under the Collaboration Agreement, we are exclusively collaborating with Novo to leverage the Company's proprietary Native Complex Platform® to discover, develop and commercialize multiple potential oral small molecule therapies for metabolic-related diseases based on certain specified molecular targets. The collaboration objective is to discover and develop several novel mono-, dual-, or triple-acting oral small molecule drug candidates directed across five GPCRs, including the GLP-1, GIP, and glucagon receptors (the "Collaboration Targets"). The collaboration included our most advanced preclinical metabolic program focused on developing an oral small molecule agonist to the GIP receptor.

After the Collaboration Agreement became effective on July 1, 2025, we and Novo commenced four simultaneous research and development programs (each an "R&D Program") with each pursuing one or more Collaboration Targets from discovery through development candidate selection. Beginning with investigational new drug-enabling activities, Novo will then be responsible for all further global development and commercialization for each product candidate at its sole cost and expense. Subject to certain limitations, Novo has the right to modify the research plans and explore additional combinations of the existing Collaboration Targets for one or more of such R&D Programs provided that no more than four R&D Programs will be pursued simultaneously. Novo reimburses us for 100% of the costs arising from all research and development activities undertaken by us under the Collaboration Agreement. Novo is also responsible for all commercialization costs subject to our profit and loss share option described below for up to one program under the collaboration.

Under the terms of the Collaboration Agreement, we will provide Novo with exclusive licenses to enable Novo to develop and commercialize products directed at the Collaboration Targets. We retain all other rights to our Native Complex Platform® and all of our other research and development programs.

In July 2025, Novo paid us a one-time, non-refundable upfront payment of $195.0 million. For each R&D Program, we are also eligible to receive up to approximately $498.0 million in research, development, regulatory, and commercial milestone payments. In addition, we are entitled to escalating, tiered royalties ranging from mid-to-high single-digits based on global product sales on a country-by-country and product-by-product basis with respect to a R&D Program until the later of ten years after the date of first commercial sale of the first product in such R&D Program in such country, expiration of specified patent rights covering such product in such country or the expiration of specified regulatory exclusivity for the first product in such R&D Program in such country. The royalty payments are subject to certain step-down provisions including reductions due to valid patent claim expiration, generic product market share on a country-by-country basis, payments made under certain licenses for third party intellectual property and application of Inflation Reduction Act maximum fair price provisions (with such cumulative reductions in most cases subject to a royalty reduction floor). Subject to certain terms, conditions and limitations, we hold an option to elect a profit and loss sharing arrangement (in lieu of milestones and royalties) for one product candidate under the Collaboration Agreement, which must be exercised by the Company within a specified time period following completion of either IND-enabling studies or the first Phase 1 clinical trial for such product.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary and novel products and product candidates. While we believe our product candidates, platform, knowledge, experience, and scientific personnel provide us with several key competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions, among others. Our future success will depend in part on our ability to maintain a competitive position with our structure-based drug discovery platform. If we fail to stay at the forefront of technological change in utilizing our platform to create and develop product candidates, we may be unable to compete effectively. Our competitors may render our approach obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and platform. Several other companies also focus on GPCRs and have platform technologies that are distinct from our Native Complex Platform®.

In addition, any product candidates that we successfully develop and commercialize, including those from our PTH1R program and SEP-631, may compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the indications that we are pursuing. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

Many of our competitors, either alone or with their collaborators, have significantly greater financial, technical, manufacturing, marketing, sales, and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the timing and scope of marketing approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage, and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive, or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. 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.

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 side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other applicable regulatory approval 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. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

Manufacturing and Supply

We do not own or operate manufacturing facilities for the production of our product candidates and currently have no immediate plans to build our own clinical or commercial scale manufacturing capabilities. We have engaged, and expect to continue to rely on, third-party CMOs to supply our product candidates for use in our preclinical studies and clinical trials.

Additionally, we intend to rely on third-party manufacturers for later-stage development and commercial manufacturing if our product candidates receive marketing approval. As our product candidates advance through clinical development, we expect to enter into longer-term commercial supply agreements to fulfill and secure our production needs. While the drug substances used in our product candidates are manufactured by more than one supplier, the number of manufacturers is limited. In the event it is necessary or advisable to acquire supplies from an alternative supplier, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company. If we need to change manufacturers during the clinical or development stage for product candidates or after commercialization for our product candidates, if approved, the FDA, European Medicines Agency ("EMA"), and other comparable foreign regulatory authorities must approve these new manufacturers in advance, which will involve testing and additional inspections to ensure compliance with FDA regulations and standards and may require significant lead times and delay. Reliance on third-party manufacturers and CMOs may expose us to different risks than if we were to manufacture and develop product candidates ourselves. Should any of these manufacturers become unavailable to us for any reason, we believe that there are a number of potential replacements, although we may incur some delay in identifying and qualifying such replacements.

We have personnel with extensive technical, manufacturing, analytical, and quality experience to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by pursuing and, once obtained, by maintaining patent protection in the United States and in selected foreign jurisdictions for our product candidates, new therapeutic approaches and potential indications, and other inventions that are important to our business. We also rely on the skills, knowledge, and experience of our scientific and technical personnel, as well as that of our advisors, consultants, contractors, and collaborators. To help protect our proprietary know-how that we elect not to patent, such as our proprietary Native Complex Platform®, processes for which patents are difficult to enforce, and any other elements of our product candidates, technology and product discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents, we rely on confidentiality and

other agreements to protect our interests. We generally require our employees, consultants, scientific advisors and contractors to enter into confidentiality agreements prohibiting the disclosure of our confidential information and requiring disclosure and assignment to us of their ideas, developments, discoveries and inventions important to our business. In addition, we also plan to rely on regulatory protection based on orphan drug exclusivities, data exclusivities, and market exclusivities. See the subsection section titled "—Government Regulation" for additional information.

The patent positions of biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific, and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will issue with respect to any patent applications that we may file in the future, nor can we ensure that any of our patents or future patents will be commercially useful in protecting our product candidates and methods of using or manufacturing the same. In addition, the coverage claimed in a patent application may be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our product candidates, if they obtain required regulatory approvals, will be protectable or remain protected by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented, or invalidated by third parties.

Our commercial success will also depend in part on our ability to operate without infringing the proprietary intellectual property rights of third parties, and in part on our ability to prevent others from infringing our proprietary rights. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our future drugs or processes, obtain licenses, or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have an adverse impact on us. See "Risk Factors—Risks Related to Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

Patent Filings

We generally file patent applications directed to our product candidates in an effort to secure our intellectual property positions vis-à-vis these programs. For our product candidates, we will, in general, initially pursue patent protection covering compositions of matter and therapeutic methods of use. Throughout the development of our product candidates, we will seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including by protecting inventions related to additional methods of use, processes of making, formulations and dosing regimens. As of March 1, 2026, we owned 2 issued patents and 135 pending patent applications in the United States, Europe, Japan, China and other territories, covering our product candidates and our research efforts. Assuming the timely payment of all applicable maintenance fees, our issued patents are projected to expire between 2044 and 2045, and our pending applications, if issued, are projected to expire between 2043 and 2046.

As of March 1, 2026, for our programs directed to small molecule agonists of PTH1R, small molecule inhibitors of MRGPRX2, and small molecule inhibitors of TSHR, and methods of using each of the foregoing, we own a total of 12 patent families. Assuming the timely payment of all applicable maintenance fees, the patents that may ultimately issue from families are projected to expire between 2043 and 2046.

Patent Term Extensions

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but cannot extend beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. If one or more of our pending United States patent applications are issued as United States patents covering our products or their therapeutic use it is possible that the patents may be entitled to patent term extensions. If a therapeutic use of a drug candidate or the drug candidate itself receives FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved use or drug candidate. We also intend to seek patent term extensions in any other jurisdictions where available. However, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted and even if granted, the length of such extensions.

Trade Secrets & Know-how

In addition to patent protection, we also rely on trade secrets, trademarks, proprietary information, confidential know-how, and continuing technological innovation to develop and maintain our competitive position. Our trade secrets, proprietary information, and confidential know-how includes our Native Complex Platform®. However, trade secrets, proprietary information, and confidential know-how can be difficult to protect. We seek to protect our trade secrets, proprietary information, and confidential know-how, in part,

using confidentiality agreements with any collaborators, scientific advisors, employees, and consultants and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors, and collaborators. These agreements may not provide adequate protection. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets, proprietary information, and confidential know-how may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop substantially the same or similar proprietary information and techniques or may otherwise gain access to our proprietary information. As a result, we may not be able to meaningfully protect our trade secrets, proprietary information, and confidential know-how. For more information regarding the risks related to our intellectual property, see the section titled "Risk Factors—Risks Related to Intellectual Property."

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union (the "EU"), extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the U.S. Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the U.S. Department of Justice or other governmental entities. In addition, an applicant may need to recall a product.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations;
- submission to the FDA of an IND which must take effect before human clinical trials may begin;
- approval by an institutional review board ("IRB") representing each clinical site before each clinical trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCPs") to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA and payment of user fees;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- FDA review and approval of the NDA; and
- compliance with any post-approval requirements, including risk evaluation and mitigation strategies ("REMS") and post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a compound in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient ("API") and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. Some long-term preclinical testing, such as animal tests of reproductive adverse effects and carcinogenicity, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of the investigational drug. In an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments. In addition, an applicant submits the results of the preclinical tests, manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. The FDA also may impose a clinical hold or partial clinical hold after commencement of a clinical trial under an IND. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation (or full investigation in the case of a partial clinical hold) may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study is conducted in accordance with GCP, including review and approval by an independent ethics committee ("IEC") and informed consent from subjects. The GCP requirements are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. FDA must also be able to validate the data from the study through an on-site inspection if necessary.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review of the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (NIH) for public dissemination on its *ClinicalTrials.gov* website.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects, or their legal representative, provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1. The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine maximal dosage.
- Phase 2. The drug is administered to a limited patient population to identify possible adverse effects ("AEs") and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product. Post-approval studies, often referred to as Phase 4 studies, may be conducted after initial regulatory approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. In addition, within 15 calendar days after the sponsor determines that the information qualifies for reporting, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as 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 drug candidate and, among other things, the applicant must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a significant application user fee as well as annual prescription drug product program fees. These fees are typically increased annually. Certain exceptions and waivers are available for some of these fees.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt, before accepting the NDA for filing, to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Applications for drugs containing new molecular entities are meant to be reviewed within 10 months from the date of filing, and applications for "priority review" products containing new molecular entities are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

During its review of an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA, including drug component manufacturing (such as APIs), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an NDA unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential AEs, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe

use ("ETASU"). ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, and Priority Review

The FDA has a number of programs intended to facilitate and expedite development and review of new drugs if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. Three of these programs are referred to as Fast Track Designation, Breakthrough Therapy Designation, and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track Designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product 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 FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate an NDA review for a priority review if it is for a product that treats a serious or life-threatening disease or condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from 10 months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality ("IMM"), and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly.

The accelerated approval pathway is contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Sponsors are also required to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the sponsor fails to conduct such studies in a timely manner and send the necessary updates to the FDA, or if a confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for product candidates approved under accelerated regulations, which could adversely impact the timing of the commercial launch of the product.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities and select clinical trial sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If a complete response letter is issued, the applicant may resubmit the NDA to address all of the deficiencies identified in the letter, withdraw the application, or request a hearing. If the applicant resubmits the NDA, the FDA will issue an approval letter only when the deficiencies have been addressed to the FDA's satisfaction. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety or effectiveness after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, reporting of adverse experiences with the product and applicable product tracking and tracing requirements. After approval, many 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 annual prescription drug product program fee requirements for certain marketed products.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the NDA holder and any third-party manufacturers that the NDA holder may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the 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 AEs of unanticipated severity or frequency, or with 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 trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. 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 voluntary product recalls;
- fines, warning or untitled letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

From time to time, legislation is drafted, introduced, passed in Congress and signed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidances, and policies are often revised or reinterpreted by the agency in ways that may significantly affect the manner in which pharmaceutical products are regulated and marketed.

Hatch-Waxman Amendments

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application ("ANDA"). An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product, known as a reference listed drug ("RLD"). ANDAs are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through *in vitro*, *in vivo*, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

Non-Patent Exclusivity

Under the Hatch-Waxman Amendments, the FDA may not approve (or in some cases accept) an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity ("NCE"). For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, which states the proposed generic drug will not infringe one or more of the already approved product's listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity for non-NCE drugs if the NDA or a supplement to the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by

or for the applicant and are essential to the approval of the application or supplement. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication, but it generally would not protect the original, unmodified product from generic competition. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it only prevents FDA from approving such ANDAs.

A drug product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods for all formulations, dosage forms, and indications of the active moiety and to patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection and 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, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval, each of the patents listed by the NDA sponsor is published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Upon submission of an ANDA or 505(b)(2) NDA, an applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book that:

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- such patent has expired;
- the date on which such patent expires; or
- such patent is invalid, unenforceable or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted.

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired. If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification the applicant must send notice of the paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. If the drug has NCE exclusivity and the ANDA is submitted four years after approval, the 30-month stay is extended so that it expires seven and a half years after approval of the innovator drug, unless the patent expires or there is a decision in the infringement case that is favorable to the ANDA applicant before then.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Amendments, which permits a patent term restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date, provided the sponsor acted with diligence. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question and within 60 days of drug approval. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office ("USPTO") reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows similar lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires a submission to the relevant competent authorities of a marketing authorization application ("MAA") and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

In the EU, an applicant for authorization of a clinical trial must obtain prior approval from the national competent authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the relevant independent ethics committee has issued a favorable opinion. In April 2014, the Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted in the EU. The Clinical Trials Regulation is directly applicable in all the EU Member States and repealed the Clinical Trials Directive 2001/20/EC, as of January 31, 2022.

The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, known as the "Clinical Trials Information System"; a single set of documents to be prepared and submitted for the application, as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by an elected Reference Member State, with support of the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (the Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure continues to be governed by the national laws of the concerned EU Member State, however overall related timelines are defined by the Clinical Trials Regulation.

Marketing Authorization

To obtain a marketing authorization for a product in the EU, an applicant must submit an MAA either under a centralized procedure administered by the European Medicines Agency ("EMA") or one of the procedures administered by competent authorities in the EU Member States (national, decentralized or mutual recognition procedure) for obtaining a marketing authorization in one or more EU Member States. A marketing authorization may be granted only to an applicant established in the European Economic Area ("EEA") (which is comprised of the EU Member States plus Norway, Iceland and Liechtenstein).

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EEA. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue-engineered products) and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of HIV, AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for other products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the centralized procedure, the Committee for Medicinal Products for Human Use ("CHMP") established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from a public health perspective and in particular from the point of view of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, excluding clock stops, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 67 days from the date of the CHMP opinion, the European Commission will adopt its final decision on the MAA.

The decentralized marketing authorization procedure allows an applicant to apply for simultaneous authorization in more than one EU Member State of medicinal products that have not yet been authorized in any EU Member State and that do not fall within the mandatory scope of the centralized procedure.

The mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of another EU Member State. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Pediatric Development

Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan ("PIP") covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the product for which a marketing authorization is being sought. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of the protection under a supplementary protection certificate ("SPC"), provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires, even where the trial results are negative. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Data and Market Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar (abbreviated) marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the EU. During an additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization 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. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained a marketing authorization based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) either (i) such condition affects no more than five in ten thousand persons in the EU when the application is made, or (ii) without the benefits derived from orphan status, it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment in its development and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product would be of significant benefit to those affected by that condition.

An orphan designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized EU marketing authorization. Marketing authorization for an orphan medicinal product leads to a ten-year period of market exclusivity being granted. During this market exclusivity period, the European Commission or the competent authorities of the EU Member States may only grant a marketing authorization to a "similar medicinal product" to the authorized orphan product for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized orphan product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized orphan product consents to a second medicinal product application; or (iii) the marketing authorization holder for the authorized orphan product cannot supply enough orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year,

it is established that the product no longer meets the criteria for orphan designation because, for example, the product is sufficiently profitable not to justify market exclusivity. Orphan designation must be requested before submitting an application for marketing authorization. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Periods of Authorization and Renewals

A marketing authorization has an initial validity of five years. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA (for a centrally authorized product) or by the competent authority of the relevant EU Member State (for a nationally authorized product). To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least nine months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authorities of the relevant Member States decide, on justified grounds relating to pharmacovigilance, to proceed with one further five year renewal period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for centrally-authorized products) or on the market of the authorizing EU Member State (for nationally-authorized products) within three years after authorization is granted, ceases to be valid (the so-called sunset clause).

Regulatory Requirements after a Marketing Authorization has been Obtained

Where an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive (EU) 2017/1572, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and APIs, including the manufacture of APIs outside of the EU with the intention to import the APIs into the EU.
- The marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of products and/or the general public, are strictly regulated in the EU notably under Directive 2001/83/EC, as amended, and EU Member State laws and industry codes of conduct.

The aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval. On December 11, 2025, the European Parliament and the European Council reached agreement on the EU Pharma Law Package, also known as the General Pharmaceutical Legislation. While he adopted acts of the new pharmaceutical legislation are expected to enter into force in 2026, the following two years, until 2028, will serve as a transition period. In this time interval, EU member states are expected to update their national laws to align with the new rules, after which the new legislation becomes applicable.

Brexit and the Regulatory Framework in the United Kingdom

The UK ceased being a Member State of the EU on January 31, 2020. Following the end of the Brexit transition period on January 1, 2021, the UK is not generally subject to EU laws in respect of medicines. The EU laws that have been transposed into UK law through secondary legislation remain applicable in the UK, however, new legislation such as the EU Clinical Trials Regulation is not applicable in the UK. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") became the UK's standalone medicines and medical devices regulator. 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 relation to Northern Ireland and introduces a UK-wide licensing process for medicines. A single UK-wide marketing authorization may be granted by the MHRA for medicinal

products intended to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK.

Review and Approval of Medicinal Products in Australia

The Therapeutic Goods Administration ("TGA") and the National Health and Medical Research Council ("NHMRC") set the GCP requirements for clinical research in Australia.

Compliance with the regulations, standards and codes set by the TGA and NHMRC is mandatory. Under the *Therapeutic Goods Act 1989* (Cth) and the *Therapeutic Goods Regulations 1990* (Cth), it is a condition (amongst other conditions) of all clinical trials involving investigational medicinal products to comply with the National Statement on Ethical Conduct in Research Involving Humans, published by the NHMRC (the National Statement), and the Guideline for Good Clinical Practice published by the International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use ("ICH Guidelines"). The ICH Guidelines have been adopted in Australia, and must be complied with across all fields of clinical research involving therapeutic goods, including those related to pharmaceutical quality, nonclinical and clinical data requirements and trial designs. The basic requirements for preclinical data to support a first-in-human trial under ICH Guidelines are applicable in Australia. Requirements related to adverse event reporting in Australia are generally similar to those required in other major jurisdictions (and there is alignment with the European Union's Clinical Trial Regulations: Regulation EU No 536/2014), although reporting timeframes may differ to other jurisdictions.

Clinical trials conducted using "unapproved therapeutic goods" in Australia, being those which have not yet been evaluated by the TGA for quality, safety and efficacy (and including unapproved indications of therapeutic goods which have otherwise been approved for use in Australia) must occur pursuant to either the Clinical Trial Notification Scheme ("CTN Scheme") or the Clinical Trial Approval Scheme ("CTA Scheme"). In each case, the trial is supervised by a Human Research Ethics Committee ("HREC"), an independent review committee constituted in accordance with the National Statement that ensures the protection of rights, safety and well-being of human subjects involved in a clinical trial. A HREC reviews, approves and provides continuing oversight of trial protocols (including any amendments), methods and materials intended to be used in obtaining and documenting informed consent of the clinical trial subjects.

The CTN Scheme broadly involves:

- the investigator or sponsor of the Australian clinical trial submitting a 'Notification of Intent to Conduct a Clinical Trial' form ("CTN Form") to the TGA and payment of the relevant fee (for unapproved medicines, this was AUD 429 at 1 July 2024: *Therapeutic Goods Regulations* 1990, clause 3, Schedule 9, item 14(a));
- the TGA may request further specific information relating to the 'unapproved therapeutic goods' that are the subject of the clinical trial;
- submission to a HREC, of all material relating to the proposed clinical trial, including the trial protocol;
- the HREC reviews the scientific validity of the trial design, the balance of risk versus harm of the therapeutic good, the ethical acceptability of the trial process, and approves the trial protocol. The HREC is also responsible for monitoring the conduct of the trial;
- the institution or organization at which the trial will be conducted, referred to as the "Approving Authority," giving final approval for the conduct of the trial at the site, in terms no less restrictive to those advised by the HREC; and
- ensuring that the CTN form is signed by the sponsor, the principal investigator, the chairman of the HREC and a person responsible from the Approving Authority. The TGA does not review any data relating to the clinical trial, however CTN trials cannot commence until the trial has been notified to the TGA. It is the responsibility of the sponsor to ensure that all relevant approvals are in place before supplying the 'unapproved' therapeutic goods in the clinical trial in Australia.

Under the CTA Scheme:

- a sponsor submits an application to conduct a clinical trial to the TGA for evaluation and comment, which includes payment of the relevant fees (for unapproved medicines, this was AUD 2,046 for a 30-day evaluation and AUD 25,426 for a 50-day evaluation, as at 1 July 2024: *Therapeutic Goods Regulations* 1990, clause 3, Schedule 9, items 1(a) and (b) respectively). The TGA encourages all sponsors to request a pre-submission meeting with the TGA in order to clarify any questions about existing studies or the proposed data package for the CTA application, and obtain specific advice from the TGA relating to the CTA application process, including the best ways to submit the application and dossier;
- the TGA will undertake a preliminary assessment to ensure that there is sufficient data to begin evaluation. If critical data is missing, the TGA may request further information;

- a sponsor must forward any comments made by the TGA Delegate to the HREC(s) at the sites where the trial will be conducted;
- the HREC is responsible for considering the scientific and ethical issues of the proposed trial protocol.

A sponsor cannot commence a trial under the CTA Scheme until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

Approval for inclusion in the Australian Register of Therapeutic Goods ("ARTG"), is required before a therapeutic good (including pharmaceutical product) may be marketed (or supplied, imported, exported or manufactured) in Australia. Exceptions apply to therapeutic goods/pharmaceutical products that are supplied, imported, and exported to and from Australia for the purposes of a clinical trial, on the basis that certain conditions are met (e.g., the trial is conducted in accordance with the CTN or CTA scheme).

Once a sponsor decides to register a therapeutic good/pharmaceutical product in Australia, in order to obtain registration of the product on the ARTG, it is required that (amongst others):

- the sponsor submits appropriate documentation, including the outcomes of clinical trials and studies, to allow the TGA to assess the quality, safety and efficacy of the therapeutic product/pharmaceutical product; and
- the sponsor submits evidence which demonstrates that the manufacture of the therapeutic product/pharmaceutical product complies with the applicable GMP requirements.

The TGA has the ultimate discretion to decide whether to include the therapeutic product/pharmaceutical product in the ARTG.

Other Healthcare Laws

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. 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;
- federal civil and criminal false claims laws, including the False Claims Act ("FCA"), which can be enforced through civil "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. 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 FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating these statutes without actual knowledge of the statutes or specific intent to violate them in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), imposes requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. 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 Physician Payments Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA") and its implementing regulations, which requires manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Department of Health and Human Services ("HHS") information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed healthcare professionals (i.e., physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and responsible individuals may be subject to imprisonment.

Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. Factors payors consider in determining coverage and reimbursement are based on whether the product 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.

In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement

rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost- effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical products, limiting coverage and the amount of reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. 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 United States. 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. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. 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.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price ("ASP") 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. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Even if we do receive a favorable coverage determination for approved products by third-party payors, coverage policies and third-party payor reimbursement rates may change at any time.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the U.S. Centers for Medicare & Medicaid Services ("CMS") may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several U.S. Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Congress has indicated that it will continue to seek new legislative measures to control drug costs.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU Member States have the option to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many

countries in the EU. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced EU Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Current and Future U.S. Healthcare Reform

In the United States, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. For example, in March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA, among other things:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they were required to offer 50 percent point-of-sale discount off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D (later increased to 70% and then later replaced altogether under the Inflation Reduction Act with the Medicare Part D manufacturer discount program); and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- The U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, and, due to subsequent legislative amendments to the statute, will remain in effect until 2032.
- The U.S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers.
- The American Rescue Plan Act of 2021 eliminates the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.
- The Inflation Reduction Act of 2022 ("IRA") included several other provisions that may impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries and impose new manufacturer financial liability on all drugs in Medicare Part D. Further, the IRA among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" for such drugs and biologics under the law and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has completed the first and second rounds of price negotiations and has announced the first and second sets of "maximum fair prices," covering a total of 25 drugs. The Medicare drug price negotiation program is currently subject to legal challenges. It is unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry.
- The One Big Beautiful Bill Act of 2025 ("OBBBA") imposed significant reductions in Medicaid funding, additional work requirements for Medicaid recipients, and more frequent reenrollment requirements, which are expected to place substantial pressure on state Medicaid budgets, reduce enrollment, and limit covered services, which could decrease utilization of, and reimbursement for, our products, if approved.
- These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The Trump Administration has issued executive orders and supported proposed regulatory initiatives in 2025 that could have a significant impact on the prices that we, or any collaborators, may receive for any approved products.

On May 12, 2025, President Trump signed an executive order directing the Secretary of HHS to set and communicate most-favored-nation ("MFN") price targets to manufacturers and propose a rulemaking plan to impose MFN pricing if "significant progress" is not made, and also directing the federal government to support regulatory paths to allow direct-to-patient sales for companies that meet these targets. The executive order further states that the Administration will take additional action (for example, examining whether marketing approvals should be modified or rescinded or considering individual drug importation waiver authorities) should manufacturers fail to offer American consumers the MFN lowest price. In July 2025, President Trump sent letters to certain pharmaceutical companies demanding that these companies extend MFN pricing to Medicaid and newly launched drugs as well as move to direct-to-consumer models priced at MFN pricing, and soliciting binding commitments by September 29, 2025. Since this time, multiple drug manufacturers have announced plans to, for certain of their drugs, lower prices to reflect similar pricing around the world, and to sell these reduced-price drugs on a direct-to-consumer purchasing platform developed by the federal government; however, it is not known what results will occur to the extent the recipients of these letters do not reduce their U.S. prices.

On December 19, 2025, CMS released two proposed rules that would incorporate MFN pricing principles into federal reimbursement for prescription drugs. The first proposal, the Global Benchmark for Efficient Drug Pricing Model ("GLOBE") for Medicare Part B, would require manufacturers of specified single source drugs and sole source biologics to pay incremental rebates based on international benchmark prices, with participation triggered for products meeting CMS's spending and eligibility criteria. The second proposal, the Guarding U.S. Medicare Against Rising Drug Costs ("GUARD") model for Medicare Part D, would similarly mandate manufacturer rebates for qualifying sole source drugs where the Medicare net price exceeds an MFN benchmark derived from international reference pricing methodologies. As proposed, GLOBE would begin a five year performance period on October 1, 2026 and GUARD would begin its performance period in 2027. These proposals will likely be subject to legal challenges that could delay their implementation or modify their impact on manufacturer pricing and revenue. Additionally, in November 2025, CMS introduced the GENErating cost Reductions fOr U.S. Medicaid ("GENEROUS") Model, a voluntary MFN framework for manufacturers participating in the Medicaid Drug Rebate Program. Although it is voluntary, the GENEROUS Model could also impact the drug pricing landscape for manufacturers.

The effect of these healthcare reform initiatives on our business and the pharmaceutical industry in general is not yet known, but could be substantial and materially adverse to our ability to successfully commercialize our product candidates at profitable price points.

Individual states have also been increasingly active in passing legislation and implementing 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. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services.

Data Protection, Privacy, and Security

In the ordinary course of business, we collect, transmit, store, use, disclose, transfer, maintain and otherwise process sensitive information, including personal data. Accordingly, we are, or may be become, subject to numerous data protection, privacy, and security obligations, including global, federal, state, and local laws, rules, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements and other obligations related to data protection, privacy, and security.

These data protection, privacy, and security obligations are evolving and may impose potentially conflicting obligations. Such obligations may include, without limitation, federal health information privacy laws, state information security and data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., the Federal Trade Commission Act). In addition, in the past few years, numerous U.S. states have passed, or are in the process of enacting, comprehensive privacy laws, rules, and regulations that impose certain obligations on covered businesses, and similar laws are being considered in several other states, as well as at the federal level. While these laws exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and are examples of the increasingly stringent and evolving regulatory frameworks related to personal data processing, as more fully discussed in the section titled "Risk Factors" included elsewhere in this Annual Report.

Additionally, to the extent we collect personal data from individuals outside of the United States, through clinical trials or otherwise, we are, or may become, subject to foreign data protection, privacy, and security laws, such as the European Union's General Data Protection Regulation ("EU GDPR") and the EU GDPR as incorporated into laws of the U.K. ("UK GDPR"). Such foreign data protection, privacy, and security laws impose significant and complex compliance obligations on entities that are subject to those laws, as more fully discussed in the section titled "Risk Factors" included elsewhere in this Annual Report.

Employees and Human Capital Resources

As of December 31, 2025, we had 130 full-time employees, 67 of whom have M.D. or Ph.D. degrees. Within our workforce, 98 employees are engaged in research and development and 32 are engaged in business development, finance, legal, and general management and administration. 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.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Corporate Information

We were incorporated under the laws of the State of Delaware in December 2019 under the name GPCR NewCo, Inc. and changed our name to Septerna, Inc. in June 2021. Our principal executive offices are located at 250 East Grand Avenue, South San Francisco, California 94080, and our telephone number is (650) 338-3533.

Our website address is *www.septerna.com*. Information that is contained in and can be accessed through our website is not incorporated into, and does not form a part of, this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Exchange Act, are available through our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Our filings with the SEC may also be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us.

All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report, including our financial statements and the related notes appearing at the end of this Annual Report and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding to invest in our common stock. If any of the events or developments described below were to occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business. This Annual Report also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See the section titled "Special Note Regarding Forward-Looking Statements."

Risks Related to Limited Operating History, Financial Position and Capital Requirements

We have a limited operating history and have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future.

Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical-stage biotechnology company with a limited operating history, which may make it difficult to evaluate the success of our business to date and assess our future viability. Since our inception in December 2019, we have focused primarily on organizing and staffing our company, business planning, establishing our intellectual property portfolio, raising capital, developing our proprietary and structure-based drug discovery platform, identifying and developing our product candidates, conducting research and preclinical studies, including IND-enabling studies, initiating and conducting clinical trials, and providing general and administrative support for these operations. Our approach to the discovery and development of product candidates based on our Native Complex Platform® is unproven, and we do not know whether we will be able to develop any product candidates that succeed in clinical development or commercially. Other than SEP-631, all of our current product candidates and development programs are in preclinical development or in the drug discovery stages. Accordingly, we have not yet successfully completed any advanced clinical trials, demonstrated an ability to successfully obtain regulatory approvals, manufactured commercial-scale product, or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our preclinical and clinical development and ongoing operations. As a result, we are not profitable and have incurred significant losses since our inception, with the exception of the year ended December 31, 2023, and negative cash flows from operating activities and capital expenditures and expect to continue to incur significant and increasing operating losses for at least the next several years. If our product candidates are not successfully developed and approved, we may never generate any significant revenue. For the year ended December 31, 2025, our net loss was $48.9 million. As of December 31, 2025, we had an accumulated deficit of $167.3 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. All of our product candidates will require substantial additional development time and resources before we would be able to apply for or receive marketing approvals and begin generating revenue from product sales. We expect to continue to incur significant losses for the foreseeable future, and we expect that our expenses will increase substantially as we continue our development of, seek marketing approval for and potentially commercialize any of our product candidates, recruit and maintain key personnel and seek to identify, assess, acquire, in-license or develop additional product candidates.

Even if we succeed in developing and obtaining marketing approval for one or more of our product candidates, we may never generate revenue that is significant enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. Our failure to become and remain profitable could decrease the value of our common stock and impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

We will require substantial additional funding in order to finance our operations. If we are unable to raise additional capital when needed on acceptable terms, or at all, we may be forced to delay, reduce, or terminate certain of our research and product development programs, future commercialization efforts or other operations.

The development of pharmaceutical product candidates, including conducting preclinical studies and clinical trials, is a very time-consuming, capital-intensive 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 identify, continue the research and development of, initiate and conduct clinical trials of, and seek regulatory approval for any product candidates we may identify. In addition, if we obtain regulatory approval for any product candidates we may identify, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reasonably estimate the actual amount of capital necessary to successfully complete the development and commercialization of our product candidates. Other unanticipated costs may also arise. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce, or eliminate our research and product development programs, future commercialization efforts or other operations.

As of December 31, 2025, we had $548.7 million in cash, cash equivalents and marketable securities. We expect that our cash, cash equivalents, and marketable securities will enable us to fund our operating expenses and capital expenditure requirements at least into 2029. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of factors currently unknown to us, and we may need to seek funding sooner than planned. Our future capital requirements will depend on many factors, including:

- the timing and progress of research and development, preclinical and clinical development activities;
- the number, scope and duration of clinical trials required for regulatory approval of our product candidates;
- the costs, timing, and outcome of regulatory review of any of our product candidates in any jurisdictions in which we or our current or any future collaborators may seek approval for our product candidates;
- the costs of manufacturing clinical and commercial supplies of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive regulatory approval;
- the costs of preparing, filing and prosecuting our patent applications, maintaining and enforcing our patents and other intellectual property rights and defending intellectual property-related claims;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements, and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- the costs of manufacturing clinical and commercial supplies of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive regulatory approval;
- the costs of preparing, filing and prosecuting our patent applications, maintaining and enforcing our patents and other intellectual property rights and defending intellectual property-related claims;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements, and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- our ability to establish and maintain collaboration and license agreements on favorable terms, if at all;
- the extent to which we acquire or in-license other product candidates and technologies;
- any product liability or other lawsuits related to our product candidates;
- our implementation of various computerized informational systems and efforts to enhance operational systems;
- expenses incurred to attract, hire and retain skilled personnel;
- the costs of operating as a public company;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payors;
- the extent to which we acquire or invest in businesses, products, and technologies;
- the effect of competing technological and market developments; and
- the impact of global economic uncertainty and geopolitical tensions, which may exacerbate the magnitude of the factors discussed above.

We expect our expenses to continue to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate preclinical studies and clinical trials of, and seek marketing approval for, product candidates, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. 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. 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. Debt 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, declaring dividends, and possibly other restrictions.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We have no committed sources of additional capital and, if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Without sufficient funding, our license agreements and any future collaboration agreements may also be terminated if we are unable to meet the payment or other obligations under such agreements.

If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate 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. Additionally, if we raise funds through additional 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 we develop, or we may have to grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock.

We have never generated revenue from product sales and may never be profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, obtain the regulatory approvals necessary to commercialize and eventually commercialize, product candidates we may identify for development. We may not generate revenues from product sales for many years, if ever. Our ability to generate future revenues from product sales depends heavily on our or our collaborators' ability to successfully:

- identify product candidates and successfully complete research and development of any product candidates we may identify;
- advance our product candidates through preclinical and clinical development;
- seek and obtain regulatory approvals for any product candidates for which we successfully complete clinical trials;
- launch and commercialize any product candidates for which we may obtain regulatory approval by establishing a sales force, marketing and distribution infrastructure, or alternatively, collaborating with a commercialization partner;
- qualify for adequate coverage and reimbursement by government and third-party payors for any product candidates for which we may obtain regulatory approval;
- establish and maintain supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for any product candidates for which we obtain regulatory approval;
- develop, maintain and enhance a sustainable, scalable, reproducible and transferable manufacturing process for the product candidates we may develop;
- address competing technological and market developments;
- negotiate favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- receive market acceptance by physicians, patients, healthcare payors, and others in the medical community;
- receive coverage and adequate reimbursement by healthcare payors;
- maintain, protect, enforce, defend and expand our portfolio of intellectual property and other proprietary rights, including patents, trade secrets and know-how;
- defend against third-party intellectual property claims of infringement, misappropriation or other violation; and
- attract, hire and retain qualified personnel.

Our expenses could increase beyond expectations if we are required by the FDA, EMA, the competent authorities of individual EU Member States, or other comparable foreign regulatory authorities to perform preclinical studies or clinical trials in addition to those that we currently anticipate. Even if one or more of the product candidates we may develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Additionally, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives. Even if we are able to generate revenues from the sale of any approved product candidates, we may not become profitable and may need to obtain additional funding to continue operations. Our failure to become and remain profitable may have an adverse effect on the value of our company and depress the market price of our common stock and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidate pipeline, achieve our strategic objectives or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Risks Related to Discovery, Development and Regulatory Approval of Product Candidates

We are early in our development efforts, and as a result it will be years before we commercialize a product candidate, if ever. If we are unable to identify and advance product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates. We are early in our development efforts and discontinued our first Phase 1 study of our prior lead candidate, SEP-786, in 2025. Other than SEP-631, for which we presented data from the Phase 1 clinical trial at the AAAAI annual meeting on March 1, 2026, our product candidates and development programs are in preclinical development or in the drug discovery stages. We have invested substantially all of our research efforts to date in developing our Native Complex Platform®, identifying potential product candidates and conducting preclinical and clinical studies. As an organization, we have limited experience in conducting and managing clinical trials necessary to obtain regulatory approvals, and we may be unable to do so for our product candidates. While we plan to continue to advance SEP-631 in clinical development, and we are also planning to advance multiple lead compounds towards selection of a next-generation oral small molecule PTH1R agonist development candidate, we have not successfully completed any advanced clinical trials to date. Additionally, we have a portfolio of targets and programs that are in earlier stages of discovery or preclinical development and may never proceed to advanced clinical-stage development. If we are able to advance these other targets and programs into advanced clinical development, we do not have experience managing multiple clinical trials simultaneously, working with global clinical trials, or working in multiple different disease indications. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for, and successfully commercializing our product candidates, either alone or with third parties, and we cannot guarantee you that we will ever obtain regulatory approval for any of our product candidates. Before obtaining regulatory approval for the commercial distribution of our product candidates, we must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates.

We may not have the financial resources to continue development of, or the ability to enter into new collaborations for, a product candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- preclinical study results may show the product candidate to be less effective than desired or to have harmful or problematic side effects;
- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by patients in our clinical trials or by individuals using product similar to our product candidates;
- our third-party manufacturers' inability to successfully manufacture our products;
- inability of any third-party contract manufacturer to scale up manufacturing of our product candidates and those of our collaborators to supply the needs of clinical trials or commercial sales;
- delays in submitting INDs or other comparable foreign applications or delays or failures in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- preclinical studies conducted outside of the United States may be affected by tariffs (including tariffs that have been or may in the future be imposed by the United States or other countries), sanctions, trade protection measures or import/export restrictions imposed by the United States or other foreign governments (including further legislation or actions taken by the United States or other countries that restrict trade);
- conditions imposed by the FDA, EMA or other comparable foreign regulatory authorities regarding the scope or design of our clinical trials;

- delays in enrolling patients in our clinical trials;
- high drop-out rates of our clinical trial patients;
- inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- inability to obtain alternative sources of supply for which we have a single source for product candidate components or materials;
- greater than anticipated costs of our clinical trials;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that no longer make a product candidate economically feasible;
- harmful side effects or inability of our product candidates to meet efficacy endpoints during clinical trials;
- failure to demonstrate a benefit-risk profile acceptable to the FDA, EMA, or other comparable foreign regulatory authorities;
- unfavorable FDA, EMA, or other comparable foreign regulatory authority inspection and review of any of the clinical trial sites or manufacturing facilities used in the testing and manufacture of any of our product candidates;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of our data by the FDA, EMA, and similar foreign regulatory authorities.

Our inability to complete development of, or commercialize our product candidates, or significant delays in doing so due to one or more of these factors, could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Preclinical and clinical drug development is a lengthy and expensive process, with uncertain timelines and outcomes. If preclinical studies or clinical trials of our product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our therapeutic candidates or any of our future therapeutic candidates on a timely basis or at all.

Successful development of pharmaceutical products involves a lengthy and expensive process, is highly uncertain, and is dependent on numerous factors, many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- clinical trial results may show the product candidates to be less effective than expected (for example, a clinical trial could fail to meet its primary or key secondary endpoint(s)) or have an unacceptable safety or tolerability profile;
- failure to receive the necessary regulatory approvals or a delay in receiving such approvals, which, among other things, may be caused by patients who fail the trial screening process, slow enrollment in clinical trials, patients dropping out of trials, patients lost to follow-up, length of time to achieve trial endpoints, additional time requirements for data analysis or New Drug Application ("NDA") or similar foreign application preparation, discussions with the FDA, EMA or other comparable foreign regulatory authorities, including FDA, EMA or other comparable foreign regulatory authorities requesting additional preclinical or clinical data (such as long-term toxicology studies), or encountering unexpected safety or manufacturing issues;
- preclinical study results may show the product candidate to be less effective than desired or to have harmful on-target or off-target side effects;
- imposition of extensive post-marketing approval requirements; or
- the proprietary rights of others and their competing products and technologies that may prevent our product candidates from being commercialized.

Furthermore, the length of time necessary to complete clinical trials and submit an application for marketing approval for a final decision by a regulatory authority varies significantly from one product candidate to the next and from one country or jurisdiction to the next and may be difficult to predict. Even if we are successful in obtaining marketing approval, commercial success of any approved products will also depend in large part on the availability of coverage and adequate reimbursement from third-party payors, including government payors such as the Medicare and Medicaid programs and managed care organizations in the United States or country-specific governmental organizations in foreign countries, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide coverage and adequate reimbursement for our products once approved, market acceptance and commercial success would be reduced. Even if we are able to obtain coverage and adequate reimbursement for our products once approved, there may be features or characteristics of our products, such as dose preparation requirements, that prevent our products from achieving market acceptance by the healthcare or patient communities.

In addition, if any of our product candidates receive marketing approval, we will be subject to significant regulatory obligations regarding the submission of safety and other post-marketing information and reports and registration, and will need to continue to comply (or ensure that our third-party providers comply) with cGMPs and GCPs for any clinical trials that we conduct post-approval. In addition, there is always the risk that we, a regulatory authority or a third party might identify previously unknown problems with a product post-approval, such as AEs of unanticipated severity or frequency. Compliance with these requirements is costly, and any failure to comply or other issues with our product candidates post-approval could adversely affect our business, financial condition and results of operations.

We may encounter substantial delays in the commencement, enrollment or completion of our planned clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing any product candidates we determine to develop on a timely basis, if at all.

The risk of failure in developing product candidates is high. It is impossible to predict when or if any product candidate would prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development, submit an IND or comparable foreign application to permit initiation of clinical studies, and then conduct extensive clinical trials to demonstrate the safety and efficacy of product candidates in humans.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our INDs and other regulatory filings. We cannot be certain of the timely identification of a product candidate or the successful completion or outcome of our preclinical testing and studies and cannot predict whether the FDA, EMA or other comparable foreign regulatory authorities will accept our proposed clinical programs or whether the outcome of our preclinical testing and studies will ultimately support the further development of any product candidates. Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. As a result, we cannot be sure that we will be able to submit INDs or other comparable foreign regulatory submissions for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs will result in the FDA, EMA, or other comparable foreign regulatory authority allowing clinical trials to begin.

Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits.

Other events that may prevent successful enrollment, initiation or timely completion of clinical development include:

- we may be unable to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in reaching a consensus with applicable regulatory authorities on trial design or implementation;
- delays in obtaining regulatory authorization to commence a clinical trial;

- delays in reaching agreement on acceptable terms with prospective CROs, other vendors, or clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different vendors and trial sites;
- delays in obtaining approval from one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional participants, or withdrawing their approval of the trial;
- delays in recruiting suitable patients to participate in our ongoing and planned clinical trials;
- changes to the clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- delays in manufacturing sufficient quantities of our product candidates for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- delays in having our product candidates being shipped on time, clearing customs and arriving at clinical trial sites intact;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- participants choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue a clinical trial;
- occurrence of AEs or SAEs associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of SAEs in clinical trials of the same class of agents conducted by other companies;
- imposition of a temporary or permanent clinical hold by regulatory authorities;
- selection of clinical trial end points that require prolonged periods of clinical observation or analysis of the resulting data;
- clinical trials producing negative or inconclusive results;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign authorities to temporarily or permanently shut down due to violations of cGMP regulations or other applicable requirements, or contamination or cross-contaminations of product candidates in the manufacturing process;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol or other regulatory requirements or committing fraud; or
- changes in regulatory requirements, guidance, or feedback from regulatory agencies that require amending or submitting new clinical protocols or otherwise modifying the design of our clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs overseeing the conduct of such trials, by a Data Safety Monitoring Board for such trial or by the FDA, EMA, or other comparable foreign regulatory authorities. Such regulatory authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, or other comparable regulatory foreign authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination and approval, which may impact the costs, timing or successful completion of a clinical trial.

Further, conducting clinical trials in foreign countries, as we have done and may continue to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocols as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory requirements, as well as political, currency exchange and other economic risks relevant to such foreign countries. Investigators and patients may not be able to comply with clinical trial protocols if quarantines or other constraints impede patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff which in turn could adversely impact our clinical trial operations. Additionally, we may experience interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel, quarantines or social distancing protocols imposed or recommended by federal or state governments, employers and others in connection with public health concerns. We may face delays in meeting our anticipated timelines for our ongoing and planned clinical trials, which could adversely affect our business, financial condition, results of operations and growth prospects.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future product sales and regulatory and commercialization milestones. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring comparable products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Serious adverse events, undesirable side effects or other unexpected properties of our product candidates may be identified during development or after approval, which could lead to the discontinuation of our clinical development programs, refusal by regulatory authorities to approve our product candidates or, if discovered following marketing approval, revocation of marketing authorizations or limitations on the use of our product candidates, any of which would limit the commercial potential of such product candidate.

To date, we have not completed the evaluation of any product candidates in advanced human clinical trials. It is impossible to predict when or if any product candidates we may develop will ultimately prove safe in humans. As is the case with pharmaceuticals generally, it is likely that there may be side effects and AEs associated with our product candidates' use. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test our product candidates in larger, longer and more extensive clinical trials with a broader group of patients, or as use of these product candidates becomes more widespread if they receive marketing approval, illnesses, injuries, discomforts and other AEs that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by participants. Many times, side effects are only detectable after investigational product candidates are tested in large-scale, Phase 3 trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates has serious or life-threatening side effects or other side effects that outweigh the potential therapeutic benefit, the development of the product candidate may fail or be delayed, or, if the product candidate has received marketing approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition. In particular, because we are developing our product candidates for chronic indications, the FDA, EMA, and other comparable foreign regulatory authorities will likely require that our product candidates demonstrate a higher level of safety over a longer period of time than would be the case for product candidates intended for short-term use. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed and our ability to generate revenue through their sale may be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial value for the product candidate if approved. We may also be required to modify our trial plans based on findings after we commence our clinical trials. Many compounds that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the compound. For example, we discontinued development of our previous lead candidate, SEP-786, following the observation of two unanticipated severe (Grade 3) events of elevated unconjugated bilirubin in the MAD portion of the Phase 1 trial.

In addition, if any of our product candidates receive marketing approval, the FDA could require us to include a boxed warning in our label or adopt a risk evaluation and mitigation strategy ("REMS"), to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the drug for distribution to patients and a communication plan to health care practitioners. For example, the FDA required that the product label for NATPARA, an approved, injectable parathyroid hormone product targeting PTH1R for the management of hypoparathyroidism include a boxed warning related to the risk of osteosarcoma based on rodent carcinogenicity studies and also implemented a REMS program to ensure patients and prescribers were appropriately counseled on the benefits and risks of the drug. Similarly, the FDA initially included boxed warnings for FORTEO and TYMLOS, injectable PTH peptides approved for osteoporosis due to the risk of osteosarcoma. While we have not yet conducted carcinogenicity studies for any of our product candidates that target PTH1R, it is possible that absent compelling data to the contrary, the FDA, EMA, and other comparable foreign regulatory authorities will similarly require a boxed warning if any product candidates we may advance to clinical development that target PTH1R are approved for marketing. Furthermore, if we or others later identify undesirable side effects caused by our product candidates, several other potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;

- regulatory authorities may require additional warnings on the label, including "boxed" warnings, 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 a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties;
- we may need to conduct a recall;
- we may be forced to suspend marketing of that product, or decide to remove the product from the marketplace; and
- the product may become less competitive, and our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, prospects, financial condition and results of operations.

Our product candidates are subject to extensive regulation and compliance obligations, which is costly and time-consuming and which may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The research, clinical development, testing, quality control, safety, effectiveness, manufacturing, labeling, packaging, storage, record-keeping, advertising, promotion, marketing, import, export, distribution, post-approval monitoring, and post-approval reporting of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable foreign regulatory authorities in foreign markets. In the United States, neither we nor any current or future collaborators are permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, new relevant statutes or regulations may be enacted, and the FDA, EMA and other comparable foreign regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA, EMA and other comparable foreign regulatory authorities, which could require us to delay or abandon clinical development plans. In addition, regulatory authorities may require us to conduct further preclinical studies before evaluating our product candidate in a clinical trial. Once we initiate clinical trials, the FDA, EMA, or other comparable foreign regulatory authorities may require additional clinical trials or suggest changes to our planned clinical trials, prior to and in support of the approval of a NDA or equivalent foreign marketing application. Changes to data requirements by the FDA, EMA, or other comparable foreign regulatory authorities during the development of our product candidates may cause the applicable regulatory authorities to require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or regulatory authorities may object to elements of our clinical development program.

The FDA, EMA or other comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA, EMA or other comparable foreign regulatory authorities for approval;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;

- the inability to demonstrate that a product candidate is safe and effective, and that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation or analysis of data from preclinical studies or clinical trials; such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- approval may be granted only for indications that are significantly more limited than what has been applied for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes, approval policies or facilities of our third-party manufacturers with which we or any of our current or future collaborators contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our current or future collaborators' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA, EMA, and other comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our current or future collaborators from commercializing our product candidates.

Of the large number of drugs in development, only a small percentage successfully complete the FDA, EMA, or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, which could adversely affect our business, operating results and prospects.

Patient enrollment and retention in clinical trials is a significant factor in the timing of clinical trials and depends on many factors, including the size and nature of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data with respect to the study drug, the number, nature and duration of competing treatments and ongoing clinical trials of competing drugs for the same indication, the proximity of patients to clinical trial sites and the eligibility criteria for the clinical trial. As our programs progress, we or our collaborators may not be able to initiate or continue clinical trials for any product candidates we identify or develop if sufficient numbers of eligible patients are unable to be located and enrolled to participate in these trials as required by the FDA, EMA, or other comparable foreign authorities, or as needed to provide appropriate statistical power for a given trial. For certain of our product candidates, the conditions which we may evaluate include rare diseases with limited patient pools from which to draw. In some cases, patient populations for rare diseases are located at specific academic sites focused on such indications, often with multiple competing clinical trials. Potential patients for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for such trials. We or our collaborators also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for the planned clinical trials and monitoring such patients adequately during and after treatment. As noted above, other pharmaceutical companies targeting these same diseases are recruiting clinical trial patients from these patient populations, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates, which may make it more difficult to fully enroll patients in clinical trials for our product candidates. In addition, the process of finding and diagnosing patients may prove costly.

The eligibility criteria of clinical trials for our product candidates, once established, may further limit the pool of available trial participants. If the actual number of patients with these diseases is smaller than anticipated, clinical trials for our product candidates may encounter difficulties in enrolling patients, thereby delaying or preventing development and approval of our product candidates. Even once a sufficient number of patients have been enrolled in a clinical trial for our product candidate, the inability to retain patients through to the study's completion may cause a failure of the study to meet its objectives and/or clinical endpoints.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on the ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment or retention in our clinical trials for a variety of reasons. Patient enrollment and retention in clinical trials depends on many factors, including:

- the size and nature of the patient population, in particular for rare diseases such as the diseases on which we are focused initially, and process for identifying patients;
- the severity of the disease under investigation;
- the design of the trial protocol;
- efforts to facilitate timely enrollment in clinical trials;
- the existing body of safety and efficacy data for the product candidate;
- the number and nature of competing treatments and ongoing clinical trials of competing therapies for the same indication;
- the proximity and availability of clinical trial sites for patients;
- the eligibility and exclusion criteria for the trial;
- the complexity of the trial, including number of office visits, lab tests, patient evaluations, and dosing regimens;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the ability to adequately monitor patients during a trial, clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied;
- the risk that enrolled patients will drop out of a trial before completing all site visits; and
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

Furthermore, our efforts to build relationships with patient communities may not succeed, which could result in delays in patient enrollment in clinical trials for our product candidates. In addition, any negative results we or our collaborators may report in clinical trials of a given product candidate may make it difficult or impossible to recruit and retain patients in other clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates, or could render further development impossible. Further, if patients drop out of clinical trials for our product candidates, miss scheduled doses or follow-up visits, or otherwise fail to follow clinical trial protocols, the integrity of data from clinical trials for our product candidates may be compromised or not accepted by the FDA, EMA, or other comparable foreign regulatory authorities, which would represent a significant setback for the applicable program. In addition, we may rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance. Such delays or failures could adversely affect our business, operating results and prospects.

Even if we receive regulatory approval of any 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.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, EMA and other comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, other marketing application and previous responses to inspection 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.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. Certain endpoint data we hope to include in any approved product labeling also may not make it into such labeling, including exploratory or secondary endpoint data such as patient-reported outcome measures. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, EMA or other comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may impose consent decrees or 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 our product candidates, including AEs of unanticipated severity or frequency, or with our third-party manufacturers 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 trials to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of 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.

Additionally, under the FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA issuing a publicly available non-compliance letter to the sponsor. The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The policies of the FDA, EMA and other comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. In addition, the U.S. Supreme Court's July 2024 decision to overturn established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. As a result of the U.S. Supreme Court's decision, the FDA and other agencies may be less inclined to engage in formal regulation and may rely to a greater degree on informal guidance, which may not always be susceptible to immediate challenge. We cannot predict the likelihood, nature or extent of government regulation or guidance that may arise from future court decisions, legislation, or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or guidance or the adoption of new requirements, guidance, or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our therapeutics may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include our expectations regarding the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial or the initiation of other clinical programs. All of these milestones are and will be based on numerous assumptions, including:

- our available capital resources or capital constraints we experience;
- the rate of progress, costs and results of clinical trials for our drug candidates and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators;
- our or our collaborators' ability to identify and enroll patients who meet clinical trial eligibility criteria;
- our or our collaborators' receipt of approvals by the FDA, EMA, and other comparable foreign regulatory authorities and the timing thereof;

- other actions, decisions or rules issued by regulators;
- our or our collaborators' ability to access sufficient, reliable and affordable supplies of materials used to manufacture our product candidates;
- the efforts of our collaborators with respect to the commercialization of our product candidates;
- the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities; and
- securing product reimbursement

The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If these milestones are not met as publicly announced, or at all, the commercialization of our product candidates may be delayed or never achieved and, as a result, our stock price may decline.

Results of preclinical studies and early clinical trials on any of our product candidates may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported AEs. In addition, while the animal models used in preclinical studies are designed to be representative of disease states in humans, these preclinical models may not be able to accurately predict the way a product candidate will affect patients in clinical trials. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen, product formulation and other clinical trial protocols and the rate of dropout among clinical trial patients. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We have limited financial and managerial resources, and to date, we have focused on research programs and product candidates within the endocrinology, immunology and inflammation, neurology and metabolic therapeutic areas. In September 2025, we selected a new PTH1R development candidate, SEP-479, and we plan to initiate a placebo-controlled, SAD and MAD Phase 1 clinical trial in Australia, pending the successful completion of regulatory submissions in the first half of 2026. Correctly prioritizing our research and development activities is particularly important for us due to the breadth of potential product candidates and indications that we believe could be pursued by leveraging our Native Complex Platform®. As a result, we may forgo or delay pursuit of opportunities with other product candidates or in other therapeutic areas that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. We must continually assess the potential commercial viability of our research programs and product candidates, and we may decide to pause or discontinue development of any of our product candidates based upon such assessments, even if we obtain positive data from our product candidates in preclinical studies and clinical trials.

Our proprietary Native Complex Platform® is based on novel technologies that are unproven and may not result in approvable or marketable products, which exposes us to unforeseen risks and makes it difficult for us to predict the time and cost of product development and potential for regulatory approval, and we may not be successful in our efforts to expand our development portfolio of product candidates.

A key element of our strategy is to use our proprietary Native Complex Platform® to overcome the historical limitations of GPCR drug development, including the isolation, purification and stabilization of GPCRs in their native forms, in order to build a robust and diverse portfolio of potentially first-in-class and best-in-class oral small molecule therapies that address both well-validated and novel GPCR targets.

The scientific research that forms the basis of our efforts to develop product candidates with our platform is still ongoing. We are not aware of any FDA approved therapeutics utilizing the technology underlying our platform. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on our platform is both preliminary and limited. As a result, we are exposed to a number of unforeseen risks and it is difficult to predict the types of challenges and risks that we may encounter during development of our product candidates. For example, we have only generated limited clinical data on our prior lead candidate, SEP-786, which led us to discontinue the program, and we have generated only limited early clinical data for SEP-631, our selective, oral small molecule MRGPRX2 NAM. Our current data on our development pipeline is limited to animal models and preclinical cell lines, the results of which may not translate into humans. Further, relevant animal models and assays may not accurately predict the safety and efficacy of our product candidates in humans, and we may encounter significant challenges creating appropriate models and assays for demonstrating the safety and purity of our product candidates.

Given the novelty of our technology, we intend to work closely with the FDA and comparable foreign regulatory authorities to perform the requisite scientific analyses and evaluation of our methods to obtain regulatory approval for our product candidates; however, due to a lack of comparable experiences, the regulatory pathway with the FDA and comparable regulatory authorities may be more complex and time-consuming relative to other more well-known therapeutics. Even if we obtain human data to support our product candidates, the FDA or comparable foreign regulatory authorities may lack experience in evaluating the safety and efficacy of product candidates like those developed using our platform, which could result in a longer than expected regulatory review process, increase our expected development costs, and delay or prevent commercialization of our product candidates. We cannot be certain that our approach will lead to the development of approvable or marketable products, alone or in combination with other therapies.

Although our research and development efforts to date have resulted in a development portfolio of potential programs and product candidates, we may not be able to discover or identify novel chemical matter to new GPCR targets and thus not be able to develop product candidates to expand our development portfolio. We may also pursue opportunities to acquire or in-license additional businesses, technologies or products, form strategic alliances or create joint ventures with third parties to complement or augment our existing business. However, we may not be able to identify any product candidates through such acquisition or in-license.

Even if we are successful in continuing to build and expand our development portfolio, the potential product candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will be successful in clinical trials or receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates, we will not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

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

From time to time, we may publicly disclose interim, preliminary or topline data from our preclinical studies and clinical trials, which are 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 trial. 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 made public. 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 clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between topline, preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the 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.

We may develop our product candidates in combination with other therapies, which would expose us to additional risks.

We may develop our product candidates in combination with one or more currently approved therapies or therapies in development. Even if any of our product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, EMA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our own products being removed from the market or being less successful commercially.

We may also evaluate our product candidates in combination with one or more other therapies that have not yet been approved for marketing by the FDA, EMA or other comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved therapies that do not ultimately obtain marketing approval.

Furthermore, we cannot be certain that we will be able to obtain a steady supply of such therapies for use in developing combinations with our product candidates on commercially reasonable terms or at all. Any failure to obtain such therapies for use in clinical development and the expense of purchasing therapies in the market may delay our development timelines, increase our costs and jeopardize our ability to develop our product candidates as commercially viable therapies. If the FDA, EMA or other comparable foreign regulatory authorities do not approve or withdraw their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with any of our product candidates, we may be unable to obtain approval of or successfully market any one or all of the product candidates we develop. Additionally, if the third-party providers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Risks Related to Commercialization, Marketing and Competition

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may invest significant resources to develop these capabilities. If we are unable to establish marketing, sales or distribution capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we as a company commercialized a product. If any of our product candidates ultimately receives marketing approval, we will be required to build a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in the markets that we target, which will be expensive and time consuming, or collaborate 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 have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Furthermore, we are currently developing products for multiple indications in different medical specialties, which will require us to build different sales and marketing capabilities that are tailored to a given product or medical specialty. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary

resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Even if any of our product candidates receive marketing approval, such product candidate may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if any of our product candidates are approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Historically, several injectable PTH peptides have been approved by the FDA and other regulatory authorities for treatment of hypoparathyroidism and osteoporosis. However, our lead product candidate is an oral small molecule agonist; to date, no such oral small molecule in this indication has been approved by the FDA or any other regulatory agency. Market participants with significant influence over acceptance of new treatments, such as clinicians and third-party payors, may not adopt new oral treatments for hypoparathyroidism or osteoporosis, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any product candidates developed by us or our existing or future collaborators. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the clinical indications and patient populations for which the product candidate is approved;
- the safety, efficacy and potential advantages compared to alternative treatments and therapies;
- the timing of market introduction of the product as well as competitive products;
- effectiveness of sales and marketing efforts;
- the strength of our or our collaborators' relationships with patient communities;
- the cost of treatment in relation to alternative treatments and therapies, including any similar generic treatments;
- the ability to offer such product for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments and therapies;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- limitations or warnings, including distribution or use of restrictions contained in the product's approved labeling;
- the availability of third-party coverage and adequate reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors and government authorities;
- the strength of marketing and distribution support;
- the inclusion of any REMS program or other restrictions included by the regulators;
- the prevalence and severity of any side effects; and
- any restrictions on the use of the product together with other medications.

The efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits of our product candidates may require significant resources and may never be successful. Because we expect sales of our product candidates, if approved, to form the basis for substantially all of our revenues for the foreseeable future, the failure of our product candidates, if approved, to find market acceptance would harm our business and could require us to seek additional financing.

Even if we are able to commercialize any product candidate, the third-party payor coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors in the United States are essential for most patients to be able to afford treatments such as our products or product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for drug treatments by governmental authorities, private health insurers and other organizations will have an effect on

our ability to successfully commercialize our products, and potentially attract additional collaboration partners to invest in the development of our product candidates. We cannot be sure that adequate coverage and reimbursement in the United States, the EU, Australia or elsewhere will be available for our products or any products that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. For more information, see the section titled "Business–Government Regulation–Coverage and Reimbursement."

Third-party payors increasingly are challenging prices charged for pharmaceutical products, medical devices and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug is available. It is possible that a third-party payor may consider our products or product candidates, if approved, and a generic drug as substitutable and only offer to reimburse patients for the generic drug. Even if we show improved efficacy or safety or improved convenience of administration with our products or product candidates, if approved, pricing of an established drug for the same or similar indication may limit the amount we will be able to charge for such product. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products or product candidates, and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs, biologics and medical devices will be covered. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs, biologics and medical devices. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products or product candidates.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our products and product candidates, if approved, and on drugs related to our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Many countries, including the EU Member States, established complex and lengthy procedures to obtain price approvals, coverage and reimbursement. These procedures vary from country to country but are commonly initiated after grant of the related marketing authorization. More particularly, in the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing systems. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced countries. Reductions in the pricing of our medicinal products in one EU Member State could affect the price in other EU Member States and, thus, have a negative impact on our financial results. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products or product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. As an example, many EU Member States review periodically their decisions concerning the pricing and reimbursement of medicinal products. The outcome of these reviews cannot be predicted and could have adverse effects on the pricing and reimbursement of our medicinal products in the EU Member States.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our products or product candidates. We expect to experience pricing pressures in connection with the sale of our products and product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs, medical devices and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary and novel products and product candidates. While we believe our product candidates, platform, knowledge, experience and scientific personnel provide us with several key competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others. Our future success will depend in part on our ability to maintain a competitive position with our structure-based drug discovery platform. If we fail to stay at the forefront of technological change in utilizing our platform to create and develop product candidates, we may be unable to compete effectively. Our competitors may render our approach obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug

discovery process that we believe we derive from our research approach and platform. Several other companies also focus on GPCRs and have platform technologies that are distinct from the Native Complex Platform®, including Nxera Pharma Co., Ltd. (formerly Sosei Heptares), Structure Therapeutics Inc., Tectonic Therapeutics, Inc., and Confo Therapeutics.

In addition, we face competition with respect to our product candidates and will face competition with respect to any other product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the indications that we are pursuing. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are aware of several pharmaceutical companies that have commenced clinical trials of product candidates or have successfully commercialized products addressing areas that we are targeting. Takeda Pharmaceuticals owns the rights to parathyroid hormone product (brand name NATPARA) for the treatment of hypoparathyroidism. NATPARA was voluntarily recalled due to manufacturing issues in September 2019 in the United States and is now only available to a limited number of patients through a Special Use Program offered by its manufacturer. In October 2022, Takeda Pharmaceuticals announced manufacturing of all strengths of NATPARA will be discontinued globally by the end of 2024. Ascendis Pharma received regulatory approval for a proprietary once-daily injectable PTH peptide, palopegteriparatide (brand name YORVIPATH), in Europe and the United States. In March 2024, AstraZeneca acquired Amolyt Pharma, who was developing eneboparatide, a proprietary, once-daily injectable PTH peptide, for hypoparathyroidism, currently in Phase 3 studies. In addition, we are aware of several academic groups and companies working on making longer-acting agonists of the PTH1R. Other companies and groups are developing or commercializing therapies for hypoparathyroidism, including Calcilytix Therapeutics, Inc. (a BridgeBio Pharma, Inc. company), Entera Bio Ltd, Extend Biosciences, Inc., and MBX Biosciences, Inc. Several companies are developing clinical-stage small molecule MRGPRX2 inhibitors, including Escient Pharmaceuticals (acquired by Incyte Pharmaceuticals in April 2024), Evommune, Inc. and BioArdis LLC. Further there are several other companies pursuing therapies for chronic spontaneous urticaria addressing other receptors of interest, such a Genentech, Inc., Sanofi, Celldex Therapeutics, Inc., Jasper Therapeutics, Inc., Novartis AG, Third Harmonic Bio, Inc., and Blueprint Medicines (a Sanofi company). For TSHR, we are aware that Byondis BV and Crinetics Pharmaceuticals are also working on research stage compounds, but they have not yet entered clinical development. In addition, several companies are working on other mechanisms to address Graves' disease, such as Immunovant, Inc., and TED, including Amgen, Inc., Viridian Therapeutics, argenx SE, Roche Holding AG, Lassen Therapeutics, Inc., Tourmaline Bio, Inc. (acquired by Novartis in October 2025), Sling Therapeutics, Inc., and Acelyrin, Inc. (merged with Alumis, Inc. in May 2025). There are also several currently approved injectable products targeting incretin receptors for the treatment of obesity or type 2 diabetes ("T2D"). These include, but are not limited to, products such as Ozempic and Wegovy (semaglutide, each marketed by Novo Nordisk A/S) for T2D and obesity, respectively, Trulicity (dulaglutide, marketed by Eli Lilly and Company) for T2D, and Mounjaro and Zepbound (tirzepatide, each marketed by Eli Lilly and Company) for T2D and obesity, respectively. There are also several injectable peptide products in development pursuing similar indications with similar mechanism of actions along with combination products, including those being developed by Amgen, Inc., AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Novo Nordisk A/S, Roche Holding AG, and Viking Therapeutics, Inc., among others. In addition, there are oral products such as Rybelsus (semaglutide, marketed by Novo Nordisk A/S) approved for patients with T2D and other oral products in development for treating obesity or T2D, including those being developed by AstraZeneca, Eli Lilly and Company, Pfizer Inc., Roche Holding AG, Structure Therapeutics Inc., and Terns Pharmaceuticals, Inc. Based on our continuing evaluations of the competitive landscape, we may decide to reallocate resources and reprioritize our development programs if we determine that a particular product candidate or target indication is no longer commercially viable or advantageous.

Many of our competitors, either alone or with their collaborators, have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the timing and scope of marketing approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. 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.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Any failure to compete effectively could harm our business, financial condition and operating results.

EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the EU Member States.

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions, including the EU. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of products is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future healthcare reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to reward improper performance is typically governed by the national anti-bribery laws of EU Member States and the Bribery Act 2010 in the United Kingdom. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom despite its departure from the EU.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in some foreign countries, including some countries in the EU, the proposed pricing for a product must be approved before it may be lawfully marketed. The requirements governing product pricing and reimbursement vary widely from country to country. For example, some EU Member States have the option to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low-priced and high-priced EU Member States, can further reduce prices. An EU Member State 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. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

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

Obtaining and maintaining marketing approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a product candidate, it does not mean that comparable foreign regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining marketing approval in one jurisdiction may negatively impact the marketing approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price to be charged for a product candidate is also subject to approval.

Obtaining foreign marketing approvals and establishing and maintaining 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 in certain countries. If we or our collaborators fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed, which would adversely affect our business, prospects, financial condition, and results of operations.

Our future growth may depend, in part, on our ability to commercialize products in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our product candidates. If we obtain regulatory approval of our product candidates and ultimately commercialize our products in foreign markets, we would be subject to additional risks and uncertainties, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- the existence of additional third-party patent rights of potential relevance to our business;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is common;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- business interruptions resulting from pandemics or similar public health crises.

If the market opportunities for any of our product candidates are smaller than we estimate, even assuming approval of a product candidate, our revenue may be adversely affected, and our business may suffer.

The precise incidence and prevalence for all the conditions we aim to address with our product candidates are unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new information may change the estimated incidence or prevalence of these diseases. The total addressable market across all of our product candidates will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of our product candidates approved for sale for these indications, the availability of alternative treatments and the safety, convenience, cost and efficacy of our product candidates relative to such alternative treatments, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Risks Related to Business Operation and Industry

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing, degree of success and cost of, and level of investment in, research, development, regulatory approval and commercialization activities relating to our product candidates, which may change from time to time;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our products;
- the cost of manufacturing our product candidates, which may vary depending on FDA, EMA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with third-party manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies or other assets;
- the level of demand for any of our product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- future accounting pronouncements or changes in our accounting policies;
- the timing and success or failure of preclinical studies or clinical trials or regulatory approval for our product candidates or any competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- potential unforeseen business disruptions that increase our costs or expenses;
- effects of macro events, such as inflation, tariffs, armed conflicts, geopolitical conflicts, pandemics, natural disasters and supply chain issues, on our business and operations; and
- the changing and volatile global economic and political environment.

In addition, from time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2025, we had 130 full-time employees. As we advance our research and development programs, we may need to further increase the number of our employees and the scope of our operations, particularly in the areas of clinical development, biology, chemistry, manufacturing, general and administrative matters related to being a public company, regulatory affairs and, if any

of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must:

- expand our general and administrative functions;
- identify, recruit, integrate, maintain and motivate additional qualified personnel;
- manage our development efforts effectively, including the initiation and conduct of clinical trials for our product candidates;
- establish and build a marketing and commercial organization; and
- improve our operational, financial and management controls, reporting systems and procedures.

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

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

We are highly dependent on the services of our senior management team and if we are not able to retain these members of our management team and recruit and retain additional management, clinical and scientific personnel, our business will be harmed.

We are highly dependent on our senior management team. In particular, we are highly dependent on the development and management expertise of Jeffrey Finer, M.D., Ph.D., our Chief Executive Officer, and the other principal members of our management, scientific and clinical team. The employment agreements we have with these officers do not prevent such persons from terminating their employment with us at any time. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. In addition, we will need to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management and to attract, on terms acceptable to us, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow.

We may not be able to attract or retain qualified personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer operating history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates and consultants than what we have to offer. If we are unable to attract, retain and motivate high-quality personnel and consultants to accomplish our business objectives, the rate and success at which we can discover and develop product candidates and our business will be limited and we may experience constraints on our development objectives.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. For example, employment of our key employees is at-will, which means that any of our employees could leave our employment at any time, with or without notice. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future marketing approvals, sales of our product candidates and our results of operations.

Our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners 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, principal investigators, CROs, consultants, vendors and collaboration partners may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (i) FDA, the national competent authorities of individual EU Member States, or comparable foreign regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, EMA, or other comparable foreign regulatory authorities; (ii) manufacturing standards; (iii) U.S. federal and state fraud and abuse and other healthcare laws and regulations, including foreign requirements; or (iv) laws that require the reporting of true and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These activities also include the improper use of information obtained in the course of clinical trials or falsification of clinical trial data, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third-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 be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other U.S. federal or non U.S. healthcare programs, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Changes in U.S. and international trade policies, particularly with respect to China, may adversely impact our business and operating results.

The U.S. government has recently made statements and taken certain actions that may lead to potential changes to U.S. and international trade policies, including imposing several rounds of tariffs and export control and sanctions restrictions affecting certain products manufactured in China. Both China and the United States have each imposed tariffs indicating the potential for further trade barriers, including the U.S. Commerce Department adding numerous Chinese entities to its Unverified List, which requires U.S. exporters to go through more procedures before exporting goods to such entities. It is unknown whether and to what extent new tariffs, export controls, or other new laws or regulations will be adopted, or the effect that any such actions would have on us or our industry. For example, in December 2025, the National Defense Authorization Act ("NDAA") for Fiscal Year 2026 was enacted, which includes Section 851, commonly referred to as the "BIOSECURE Act." The BIOSECURE Act restricts U.S. government agencies from procuring certain biotechnology equipment or services from, or entering into contracts with, entities that use biotechnology equipment or services from designated "biotechnology companies of concern," which include WuXi AppTec and WuXi Biologics, or collectively WuXi, and from expending certain federal loan or grant funds for such equipment or services. While the BIOSECURE Act is primarily directed at U.S. government procurement and funding and has not yet been fully implemented through final regulations, there remains a continued policy interest in limiting U.S. companies' relationships with biotechnology providers with relationships with foreign adversaries. The potential downstream adverse impacts on entities having only commercial relationships with any impacted biotechnology providers is unknown but may include supply chain disruptions or delays. Sustained uncertainty about or further escalating trade and political tensions between the U.S. and China may prevent or hinder the export of materials or technical information among us, our contract development and manufacturing organizations ("CDMOs") and other relevant third parties, such as pharmaceutical partners, or could result in trade or retaliatory restrictions that may hinder or potentially inhibit our ability to rely on CDMOs and other service providers that operate in China. Further, regulatory or legislative action taken by the U.S. to impose restrictions on transactions with China, like the restrictions described above, could have the potential to severely restrict the ability of companies like ours to contract with Chinese biotechnology companies of concern, which could have adverse effects on the development of our product candidates and our business operations. See the risk factor titled "Risks Related to Government Regulatory and Legal Requirements—We rely on third-party manufacturers, CROs, CMOs, and suppliers to supply, develop and test components of our product candidates. The loss of our third-party manufacturers, CROs, CMOs, or suppliers, their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, or changes in methods of product candidate manufacturing, development or formulation would materially and adversely affect our business."

Any unfavorable government policies on international trade, such as export controls, economic, sanctions, capital controls or tariffs, may increase the cost of manufacturing our product candidates and platform materials, affect our ability to commercialize our product candidates if approved, the competitive position of our product candidates, and import or export of raw materials and finished product candidate used in our preclinical studies and clinical trials, particularly with respect to any product candidates and materials that we import from China, including pursuant to our service arrangements with WuXi. If any new tariffs, export controls, sanctions, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if either the U.S. or

Chinese government takes retaliatory trade actions due to the recent trade tensions, such changes could have an adverse effect on our business, financial condition and results of operations.

Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of any product candidates we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of any product candidates we may develop in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have not completed the evaluation of any product candidates in human clinical trials or that have been approved for commercial sale, the future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend any related litigation;
- a diversion of our management's time and our resources;
- exhaustion of any available insurance and our capital resources;
- initiation of investigations by regulators;
- the inability to commercialize any product candidates that we may develop;
- injury to our reputation and significant negative media attention; and
- a decline in price of our common stock.

If we continue to commence clinical trials or if we commence commercialization of any product candidates, we may seek to increase our insurance coverage. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If and when coverage is secured, our insurance policies may also have various exclusions and we may be subject to a product liability claim for which we have no coverage. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous foreign, federal, state and local environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources, including any available insurance. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities.

We could incur significant costs and liabilities which may adversely affect our financial condition and operating results for failure to comply with such laws and regulations, including, among other things, civil or criminal fines and penalties, property damage and personal injury claims, costs associated with upgrades to our facilities or changes to our operating procedures, or injunctions limiting or altering our operations.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations, which are becoming increasingly more stringent, may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Since our inception, we have incurred losses and we may never achieve profitability. As of December 31, 2025, we had $45.8 million of federal net operating loss ("NOL") carryforwards and $77.9 million of state NOL carryforwards, available to reduce future taxable income. To the extent that we continue to generate taxable losses, under current law, our unused U.S. NOLs may be carried forward to offset a portion of future taxable income, if any. Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to offset a portion of future taxable income, if any, subject to expiration of such credit carryforwards. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended ("Code"), if a corporation undergoes an "ownership change," generally defined as one or more stockholders or groups of stockholders who own at least 5% of the corporation's equity increasing their equity ownership in the aggregate by more than 50 percentage points (by value) over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Similar rules may apply under state tax laws. Our prior equity offerings and other changes in our stock ownership may have resulted in such ownership changes in the past. In addition, we may experience ownership changes in the future due to shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs or other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us and could require us to pay U.S. federal income taxes earlier than would be required if such limitations were not in effect. There is a risk that due to changes under the tax law, regulatory changes or other unforeseen reasons, our existing NOLs or business tax credits could expire or otherwise be unavailable to offset future income tax liabilities. At the state level, there may also be periods during which the use of NOLs or business tax credits is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, under Senate Bill 167 enacted by California in June 2024, generally, there is a suspension of the NOL deduction for tax years beginning on or after January 1, 2024, and before January 1, 2027 for individual and corporate taxpayers with net business income or modified adjusted gross income of $1 million or more, and a limit of $5 million of business credits on the aggregate use of otherwise allowable business tax credits that any individual or corporate taxpayer could claim for tax years beginning on or after January 1, 2024, and before January 1, 2027. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs or tax credits, even if we attain profitability.

We have and may in the future engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

We have and in the future, we may consider strategic transactions, such as acquisitions of companies, asset purchases, and in-licensing or out-licensing of products, product candidates or technologies from time to time. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our senior management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- up-front, milestone and royalty payments, equity investments and financial support of new research and development candidates including increase of personnel, all of which may be substantial;
- exposure to unknown liabilities, including potential indemnification claims from a potential spin-off or out-license of certain of our intellectual property rights;

- disruption of our business and diversion of our management's time and attention to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher than expected costs in risk-sharing collaborations;
- higher-than-expected acquisition and integration costs;
- lower-than-expected benefits, from out-licensing or selling our technology or intellectual property or from in-licensing intellectual property or purchasing assets;
- write-downs of assets or goodwill or impairment charges;
- difficulty and cost in combining or separating the operations and personnel of any acquired or sold businesses with our existing operations and personnel;
- we may disagree with our strategic partners about decisions affecting the business, which could result in litigation or arbitration that increases our expenses, distracts our officers and directors and disrupts the day-to-day operations of the strategic venture, including by delaying important decisions until the dispute is resolved;
- our strategic partners may take actions that we oppose;
- our strategic partners might experience financial distress or become bankrupt;
- impairment of relationships with key suppliers or customers of any acquired or sold businesses due to changes in our senior management and ownership; and
- inability to retain key employees of any acquired businesses.

In addition, to the extent we enter into a strategic transaction that includes ongoing operations or shared ownership and management, our strategic partners may take actions that we oppose or we may disagree with our strategic partners about decisions affecting the business, which could result in litigation or arbitration, distract our officers and directors and otherwise disrupt the day-to-day operations of our business and the business of the strategic partner or entity. Furthermore, to the extent that our directors and officers serve on the boards of our strategic partners, such directors may be required to abstain from board decision-making in the event of a conflict of interest.

Accordingly, although we cannot be certain that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks, and could harm our business, results of operations, financial condition and prospects.

We have conducted and may continue to conduct, clinical trials for our product candidates outside of the United States, and we may do so for our other product candidates. However, conducting trials outside of the United States exposes us to additional risks, which could materially harm our business.

We have conducted, and may in the future conduct, certain of our clinical trials at centers outside of the United States. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or another comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. For example, in cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; 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 inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and 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 authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trial conducted outside for the United States or the applicable jurisdiction, and the FDA has discussed proposals to increase user fees for marketing applications containing certain foreign clinical data. If the FDA, the EMA, the U.K. Medicines and Healthcare products Regulatory Agency, or other foreign regulatory authorities do not accept any data generated from other jurisdictions, we would likely be required to conduct additional clinical trials, which would be costly and time consuming, and delay aspects of our development plan, which could harm our business.

Conducting trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

If our information systems or data, or those of third parties with whom we work, are or were compromised, we could experience adverse consequences from such compromises, such as damage to our reputation, significant financial and legal exposure, or other adverse effects to our business.

We rely on information technology systems that we or third parties with whom we work, operate to process, transmit and store electronic information, including sensitive information, in our day-to-day operations. For example, in connection with our product development efforts, we may collect and process a variety of personal data, proprietary information, trade secrets, and clinical trial information. As a result, we and the third parties with whom we work, face a variety of evolving threats that could cause cybersecurity incidents, data breaches, or other adverse security events.

Cyberattacks, malicious internet-based activity, online and offline fraud, and other similar activities could result in the theft or destruction of intellectual property, personal data, or other misappropriation of assets, or otherwise threaten to compromise our confidential or proprietary information and disrupt our operations. Attempts to disrupt or gain unauthorized access to our and our third-party vendors' information systems from malicious third parties or insider threats may incorporate widely varying and frequently changing tactics, which may be enhanced or facilitated by artificial intelligence ("AI"). Such threats are increasing in their frequency, sophistication, and intensity, have become increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, intentional or inadvertent wrongful conduct by personnel and vendors (such as through human error, theft or misuse), sophisticated nation states, and nation-state-supported actors. Some actors now engage and are expected to continue to engage in cyberattacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities, wrongful conduct by hostile foreign governments and industrial espionage. During times of war and other major conflicts, we and the third parties with whom we work may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our services.

We and the third parties with whom we work are subject to a variety of evolving threats, including but not limited to the deployment of harmful malware (including as a result of advanced persistent threat intrusions), ransomware, denial-of-service, credential stuffing, credential harvesting, social engineering fraud (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), personnel misconduct or error, ransomware attacks, 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 evolving technologies, such as AI, telecommunications failures, earthquakes, fires, floods, and other similar threats.

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.

A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, there can be no assurance that our efforts will prevent information cybersecurity incidents or data breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition.

Remote work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit and in public locations. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired

or integrated entities' systems and technologies. Furthermore, we may discover security issues or other constraints not found during due diligence of such acquired or integrated entities, creating additional challenges to integrate said information systems into our information technology environment and security program.

Like other companies in our industry, we, and our third party vendors, have experienced threats and cybersecurity incidents relating to our information technology systems and infrastructure. While we have implemented security measures designed to protect against cybersecurity incidents and data breaches, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate, and remediate known vulnerabilities in our information systems (such as our hardware and/or software, including that of third parties with whom we work). We may not, however, detect and remediate all such vulnerabilities on a timely basis for various reasons including but not limited to the impact on the functional operations of affected information systems or the availability of a solution for the impacted technology. While remedial measures and/or patches designed to address identified vulnerabilities are being developed and/or implemented, these vulnerabilities could be exploited and result in a cybersecurity incident or data breach.

Applicable data privacy and security obligations may require us to notify relevant stakeholders, including affected individuals, customers, regulators, and investors, of cybersecurity incidents and data breaches. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. Additionally, laws in all 50 states require businesses to provide notice to customers whose personal data has been disclosed as a result of a data breach. These laws are not consistent, and compliance in the event of a widespread cybersecurity incident or data breach is difficult and may be costly. We also may be contractually required to notify patients or other counterparties of a cybersecurity incident or data breach. Although we may have contractual protections with our service providers, any actual or perceived cybersecurity incident or data breach could harm our reputation and brand, expose us to potential liability or require us to expend significant resources on data security and in responding to any such actual or perceived cybersecurity incident or data breach. Any contractual protections we may have from our service providers may not be sufficient to adequately protect us from any such liabilities and losses, and we may be unable to enforce any such contractual protections. In addition to government regulation, privacy advocates and industry groups have and may in the future propose self-regulatory standards from time to time. These and other industry standards may legally or contractually apply to us, or we may elect to comply with such standards. Determining whether personal data has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. Any failure, or perceived failure, to prevent or mitigate cybersecurity incidents, data breaches or other improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e.g., state breach notification laws), federal (e.g., Health Insurance Portability and Accountability Act of 1996), and foreign (e.g., the GDPR) laws, and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business, results of operations and financial condition.

While we maintain insurance coverage, we cannot assure that such coverage will be adequate or otherwise protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or material adverse effects arising out of our data protection, privacy, and security practices, or that such coverage will continue to be available on acceptable terms or at all. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

In addition, our reliance on the computer systems of various third parties with whom we work, including our CROs and other contractors, introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We rely on our third-party partners to implement effective security measures and identify and correct for any such failures, deficiencies, cybersecurity incidents or data breaches. However, 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. Any failure by such third parties to prevent or mitigate cybersecurity incidents, data breaches or other improper access to or disclosure of such information could have similarly adverse consequences for us. 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.

In addition to experiencing a cybersecurity incident or data breach, third parties may gather, collect, or infer sensitive data about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, sensitive data of the Company could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel's, or vendors' use of generative AI technologies.

Any of the previously identified or similar threats could cause a cybersecurity incident, data breach, or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or

access to our sensitive data or our information technology systems, or those of the third parties with whom we work. A cybersecurity incident, data breach, or other interruption could disrupt our ability (and that of third parties with whom we work) to provide our services.

Risks Related to Government Regulatory and Legal Requirements

Disruptions at the FDA, SEC and other U.S. government agencies caused reduction in staffing, by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of business may relay, which could negatively impact our business.

Federal agencies in the U.S., including the FDA, the SEC and other comparable regulatory authorities, operate pursuant to annual appropriations and other political and budgetary processes, and may from time to time be subject to continuing resolutions, funding lapses, or other fiscal constraints. Currently, although the FDA and many other federal agencies have funding sufficient to continue their activities through September 30, 2026, the timing and amount of future funding is unpredictable. Without appropriation of sufficient funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. The ability of the FDA, EMA, and other comparable regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's or other comparable regulatory authorities' ability to perform routine functions. Average review times at the FDA and other comparable regulatory authorities have fluctuated in recent years and may continue to fluctuate as a result of these factors. In addition, government funding of the SEC and other U.S. government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, including executive and congressional priorities, which is inherently fluid and unpredictable. For example, the Trump Administration has issued executive orders seeking to greatly reduce the size of the federal workforce, including through layoffs and severance packages offered to employees of federal agencies within the executive branch and independent agencies, including the FDA. Any such reduction in personnel may result in longer review times by the FDA and other agencies.

Disruptions at the FDA, the SEC and other agencies, including as a result of substantial leadership changes, personnel cuts, policy changes or otherwise, may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. Changes and cuts in FDA staffing have been reported by some in the pharmaceutical industry as creating delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all.

Over the last several years, including from October 1, 2025 to November 12, 2025, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and cease critical activities.

If a prolonged government shutdown occurs again, or a widespread freeze on federal funding occurs in the future or if global health concerns or staffing changes prevent the FDA, SEC, EMA, or other comparable foreign regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, including formal and informal interactions with product developers, it could significantly impact the ability of the FDA, SEC, EMA, or other such comparable foreign regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns and/or substantial leadership, personnel, and policy changes at the SEC could impact our business by delaying review of our public filings, which in turn could delay or frustrate our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations or delay the review or effectiveness of required regulatory or securities filings.

We may not be able to obtain orphan drug designation or exclusivity for our product candidates for which we seek such a designation or exclusivity, and even if we do, that designation may not provide an expedited development or regulatory review or approval process and any orphan drug exclusivity we may receive for approved products may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition. A similar regulatory scheme governs the designation of orphan product candidates by the EMA in the EU. Generally, if a product with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA (as applicable) from approving another marketing authorization application for another similar product candidate for the same orphan therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the EU (which can be extended to 12 years if the sponsor complies with an agreed-upon pediatric investigation plan). The exclusivity period in the EU can be reduced to six

years if at the end of the fifth year it is determined that a product no longer meets the criteria for orphan designation, including if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our product candidates, the agency must find that the product candidate is indicated for the treatment of a condition or disease that affects fewer than 200,000 individuals in the United States or that affects 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product candidate available for the disease or condition will be recovered from sales of the product in the United States. Hypoparathyroidism is a disease that affects approximately 70,000 individuals in the United States, and accordingly, any product candidate we advance forward in development for hypoparathyroidism may qualify for orphan drug designation. However, the FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. In the EU, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA or the EMA can subsequently approve the same product candidate for the same condition if the FDA or EMA (as applicable) concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

While we may in the future seek designations for our product candidates with the FDA, EMA and other comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process, an accelerated regulatory pathway or regulatory exclusivity, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA, EMA, and other comparable foreign regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. However, there can be no assurance that we will successfully obtain such designations for our product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Fast Track Designation for one or more of our product candidates. If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and a Fast Track Designation does not make approval more likely to occur. The FDA may rescind the Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development activities.

In the EU, we may seek to participate in the PRIority MEdicines ("PRIME") scheme for our potential product candidates. The PRIME scheme is intended to encourage development of product candidates in areas of unmet medical need and provides accelerated assessment of product candidates representing substantial innovation, where the marketing authorization application will be made through the centralized procedure in the EU. Eligible products must target conditions for which there is an unmet medical need (i.e. no treatment option exists in the EU or the applicable product candidate can offer a major therapeutic advantage over existing treatments). Many benefits accrue to sponsors of product candidates with access to the PRIME scheme, 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 the possibility of accelerated assessment of a marketing authorization application once a dossier has been submitted. There is no guarantee, however, that our potential product candidate would be deemed eligible for the PRIME scheme and even if we do participate in the PRIME scheme, where during the course of development a product no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

We may seek Breakthrough Therapy Designation for one or more of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval and priority review.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if any product candidate we develop qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation.

Even in the absence of obtaining Fast Track and/or Breakthrough Therapy Designations, a sponsor can seek priority review at the time of submitting a marketing application. The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months. Priority review designation may be rescinded if a product no longer meets the qualifying criteria.

Where appropriate, we may secure approval from the FDA, EMA, or other comparable foreign regulatory authorities through the use of expedited approval pathways, such as accelerated approval. If we are unable to obtain such approvals, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, EMA, or other comparable foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA, or other comparable foreign regulatory authorities may seek to withdraw the accelerated approval.

Where possible, we plan to pursue accelerated development strategies in areas of high unmet need. We may seek an accelerated approval pathway for our one or more of our product candidates from the FDA, EMA, or other comparable foreign regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send status updates on such studies to the FDA every 180 days to be publicly posted by the agency, or if such post-approval studies fail to verify the drug's predicted clinical benefit. The FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress.

Prior to seeking accelerated approval, we would seek feedback from the FDA, EMA, or other comparable foreign regulatory authorities and would otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA or BLA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent feedback from the FDA, EMA, or other comparable foreign regulatory authorities, we will continue to pursue or apply for accelerated approval or any

other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval, there can be no assurance that such application will be accepted or that any approval will be granted on a timely basis, or at all. The FDA, EMA, or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type, including, for example, if other products are approved via the accelerated pathway and subsequently converted by FDA to full approval. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We are subject to stringent and evolving U.S. and foreign laws, rules, regulations, policies, industry standards, contractual requirements, and other obligations related to data protection, privacy, and security. Our actual or perceived failure to comply with such obligations could adversely affect our business.

We are subject to various data protection, privacy, and security laws, rules, regulations, policies, industry standards, contractual requirements, and other obligations that apply to our collection, transmission, storage, use, disclosure, transfer, maintenance and other processing of sensitive information, including personal data. The legislative and regulatory landscape for data protection, privacy, and security continues to evolve across jurisdictions worldwide. For example, in the United States, federal, state, and local governments have enacted numerous data protection, privacy, and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws).

At the federal level, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act, and implementing regulations, establish stringent privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Further, failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission ("FTC") Act, 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities.

Regulators and legislators in the U.S. are also increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, the Department of Justice's January 8, 2025, rule on "Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons," prohibits data brokerage and data sharing transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions, and may result in exclusion from participation in federal and state programs.

Data protection, privacy, and security obligations remain an evolving landscape at both the domestic and foreign level, with new laws, rules and regulations coming into effect, posing continued legal and compliance challenges. For example, as of January 2026, twenty 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 conduct our operations. 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, in California, the California Consumer Privacy Act, as amended by the California Privacy Rights Act (collectively, "CCPA"), provides for fines of up to $7,500 per intentional violation and allows privacy 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, the third parties with whom we work.

The existence of comprehensive privacy laws in different states adds additional complexity, variation in requirements, processing restrictions and potential legal risk, requiring additional investment of resources in our compliance programs. These laws may also impact our business strategies, result in increased compliance costs and/or changes to our business practices and policies and increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

Several states are also specifically regulating consumer health information. For example, Washington has enacted a consumer health privacy law, the My Health My Data Act ("WMHMDA"), which went into effect on March 31, 2024 and regulates the collection and sharing of consumer health information. WMHMDA places restrictions on processing consumer health data (including imposing stringent requirements for consents), provides consumers certain rights with respect to their health data, and creates a private right of action to allow individuals to sue for violations of the law, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states, including Illinois and Texas, have passed laws that regulate biometric data specifically. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there have been discussions in the U.S. Congress of new comprehensive federal data privacy laws to which we could become subject to, if enacted.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data protection, privacy, and security. For example, if we conduct clinical trials in the European Economic Area ("EEA") and/or the United Kingdom ("U.K."), we may become subject to additional privacy laws in those jurisdictions, such as the EU General Data Protection Regulation ("EU GDPR") and the EU GDPR as incorporated into the laws of the U.K ("U.K. GDPR" and, together with the EU GDPR, "GDPR"), both of which impose strict requirements for processing personal data. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to having a legal basis or condition for processing personal data, stricter requirements relating to the processing of sensitive data (such as health data), where required by the GDPR obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, requiring data protection impact assessments for high risk processing and taking certain measures when engaging third-party processors.

Under the GDPR, data protection authorities may impose large penalties for violations of the GDPR, including potential fines of up to €20 million (£17.5 million GBP) or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Non-compliance could also result in the imposition of orders to stop data processing activities, which could have a material adverse effect on our business, financial position, and results of operations.

In addition, we may be unable to transfer personal data from the EEA, U.K., and other jurisdictions to the U.S. or other countries due to data localization requirements or limitations on cross-border data flows. Although there are various mechanisms that may be used in some cases to lawfully transfer personal data to the U.S. or other countries, these mechanisms are subject to legal challenges and may not always be available to us. For example, the GDPR requires certain adequate safeguards to enable the transfer of personal data outside of the EEA or the U.K., in particular to the U.S., such as the EU standard contractual clauses, U.K. International Data Transfer Addendum/Agreement, and the EU-U.S. Data Privacy Framework ("Framework") and the U.K. extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework). However, 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. If there is no lawful manner for us to transfer personal data from the EEA, the U.K. or other jurisdictions to the U.S., or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business.

Although the U.K. is regarded as a third country under the EU GDPR, the European Commission has issued a decision recognizing the U.K. as providing adequate protection under the EU GDPR, or the Adequacy Decision, and, therefore, transfers of personal data originating in the EEA to the U.K. remain unrestricted. In December 2025, the European Commission adopted a decision to extend the validity of the U.K. Adequacy Decision for six years until December 2031, determining that the U.K. continues to offer a level of data protection that is "essentially equivalent" to the EU standards. This follows the U.K.'s adoption of the Data (Use and Access) Act 2025 (the "DUAA") on June 19, 2025. The U.K. government has confirmed that personal data transfers from the U.K. to the EEA remain free flowing. The respective provisions and enforcement of the EU GDPR and U.K. GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. This lack of clarity on future U.K. laws and regulations and their interaction with EU laws and regulations could add legal risk, complexity and cost to our handling of personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the U.K. and the EEA.

In the EEA, the NIS 2 Directive ("NIS 2") is replacing the cybersecurity legal framework under the current NIS framework, aiming to ensure a high level of cybersecurity in the region. NIS 2 brings new medium and large organizations providing services in the EEA within scope of the legal framework. It extends to additional sectors and expands the list of in-scope healthcare organizations, including to certain providers engaged in research and development of medicinal products. The new regime imposes direct obligations

on management in respect of an in-scope organization's compliance with NIS 2, requires covered organizations to put in place certain cyber risk management measures, strengthens incident reporting requirements and provides supervisory authorities with a greater oversight. The majority of obligations will come into force when national legislation implementing NIS 2 becomes effective in the relevant EU Member State. EU Member States had until October 17, 2024 to transpose NIS 2 into national legislation, although many countries have still not completed the transposition. As such, the cybersecurity regulatory landscape in the EU is currently fragmented and uncertain. To the extent we are subject to NIS 2, we will require additional investment of our resources in compliance programs. Under NIS 2 companies may be subject to administrative fines of up to the higher amount of €10 million or 2% of worldwide turnover.

Furthermore, if we fail, or are perceived to have failed, to comply with applicable data protection, privacy, and security laws, including applicable HIPAA privacy and security standards, we could face significant administrative, civil and criminal penalties. For example, HHS has the discretion to impose significant penalties, and such enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the data protection, privacy, or security of the personal data of state residents. We cannot be sure how these laws, rules and regulations will be interpreted, enforced, or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws, rules and regulations at the international, federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

Additionally, we rely on certain third-party vendors to process certain confidential, sensitive, or personal data on our behalf. Failure by us or our third-party vendors to comply with any of these laws, rules, regulations, contractual requirements, industry standards, or other obligations could result in notification obligations, enforcement actions, regulatory investigations or inquiries, significant fines, imprisonment of company officials and public censure, litigation and claims for damages by affected individuals, customers or business partners, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

Our employees and personnel use generative artificial intelligence technologies to perform their work, and the disclosure and use of personal data in generative artificial intelligence technologies is subject to various privacy laws and other privacy obligations.

Our use of new and evolving technologies, such as artificial intelligence, may present risks and challenges that can impact our business, including by posing cybersecurity and other risks to our confidential and/or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability.

We, and our third-party vendors, may use and integrate AI into our business processes both in our own development and implementation of AI as well as through the adoption of commercially available tools. Use of this technology could pose cybersecurity, data privacy, IT, intellectual property, regulatory, legal, operational, competitive, reputational and other risks and challenges that could affect our business. Specifically, risks related to accuracy, bias, AI hallucinations, discrimination, harmful content, misinformation, fraud, scams, targeted attacks (including model poisoning or data poisoning), surveillance, data leakage, inequality, environmental harms, and other harms may flow from our development, use, or deployment of AI technologies. If we enable or use solutions that draw controversy due to perceived or actual negative societal impact, we may also experience brand or reputational harm, competitive harm or legal liability.

A growing number of legislators and regulators are adopting laws and regulations and have focused enforcement efforts on the adoption of AI, and use of such technologies in compliance with ethical standards and societal expectations. These developments may increase our compliance burden and costs in connection with use of AI and lead to legal liability if we fail to meet evolving legal standards or if use of such technologies results in harms or other causes of action we did not predict. For example, Europe began implementing its EU Artificial Intelligence Act ("AI Act") on August 1, 2024, with a significant part of the law scheduled to come into effect in August 2026. As currently enacted, the AI Act, which may be amended as part of the EU's Digital Omnibus, imposes significant obligations on providers and deployers of AI systems, and encourages providers and deployers of AI systems to account for EU ethical principles in their development and use of these systems. The scope of requirements depends on legal and risk determinations that rely on novel legal provisions that have not yet been interpreted by courts or regulators, and non-compliance can lead to significant fines.

In the U.S., the AI regulatory environment is complex and uncertain. Over the past year, states have advanced, and in some cases passed, dozens of laws focusing on AI governance and regulation, including on deployment of AI in healthcare settings. At the federal level, the Trump Administration has endorsed a federal moratorium on the enforcement of state AI laws, including through a December 11, 2025, executive order on "Ensuring a National Policy Framework for Artificial Intelligence." So far, these efforts have not been successful at curtailing state action on AI regulation, contributing to a complicated legislative patchwork, which may be litigated in state and federal courts. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The FDA, for example, issued guidance on the use of AI in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use AI systems governed by these laws or regulations, we will need to meet higher standards of data quality, transparency, monitoring and human oversight, and we would need to adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements, with the potential for significant enforcement or litigation in the event of any perceived non-compliance.

The rapid evolution of AI will require the application of significant resources to design, develop, test and maintain such systems to help ensure that AI is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. The use of certain AI technologies can also give rise to intellectual property risks, including by disclosing or otherwise compromising our confidential or proprietary intellectual property, or by undermining our ability to assert or defend ownership rights in intellectual property created with the assistance of AI tools.

Our vendors may in turn incorporate AI tools into their offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. In addition, the use of generative AI models in our internal or third-party systems may create new attack surfaces or methods for adversaries, which could impact us and our vendors. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

All of these compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. Our efforts to comply with the evolving data protection, privacy, AI and security laws, rules, regulations, and other obligations may be unsuccessful. We may need to devote significant resources to understanding and complying with this changing landscape. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects. Any actual or perceived failure by us or our third-party partners to comply with such laws, rules, regulations, and other obligations regarding data protection, privacy, AI and security could result in significant government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, rules or regulations, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity. Further, any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

Additionally, the hardware, software, data and cloud computing platforms that we rely on may not continue to be available at reasonable prices, on commercially reasonable terms or at all. Any loss of the right to use any of these hardware, software, data or cloud computing platforms could significantly increase our expenses and disrupt or otherwise result in delays in the provisioning of our services until equivalent technology is either developed by us, or, if available, is identified, obtained through purchase or license and integrated into our services, and no assurance can be provided that such equivalent technology would be developed or obtained in a timely manner or at all. Moreover, as a result of the increasing use and deployment of AI technologies, infrastructure capacity requirements, including network capacity and, computing power and energy requirements, may increase which could lead to an increase in serve interruptions we experience.

Healthcare legislative reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. For more information, see the section titled "Business–Government Regulation–Current and Future U.S. Healthcare Reform."

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry.

The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. In addition, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent 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, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

In August 2022, the Inflation Reduction Act of 2022 ("IRA") was signed into law. The IRA includes several provisions that may impact our business, depending on how various aspects of the IRA are implemented. Provisions that may impact our business include a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, the imposition of new manufacturer financial liability on most drugs in Medicare Part D, permitting the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, requiring companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general is not yet known.

We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We cannot predict what healthcare reform initiatives may be adopted in the future. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government 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 drugs.

Our relationships with customers, physicians, and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, other healthcare laws and regulations and health data privacy and security laws and regulations, contractual obligations and self-regulatory schemes. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors may subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our clinical research, as well as our proposed sales and marketing programs. In addition, we may be subject to health information privacy and security laws by the federal government, the states and other jurisdictions in which we may conduct our business. For more information, see the section titled "Business–Government Regulation–Other Healthcare Laws."

Because of the breadth of these laws and the limited statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations.

Legislation or other changes in U.S. tax law may have a material adverse effect on our business, cash flow, financial condition, or results of operations.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. For example, the One Big Beautiful Bill Act ("H.R.1") was signed into law on July 4, 2025 and made significant changes to U.S. federal tax law. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. For example, under Section 174 of the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development performed outside the U.S. will be capitalized and amortized, which may have an adverse effect on our cash flow. H.R.1 provides that for taxable years beginning after December 31, 2024, expenses that are incurred for research and development performed in the U.S. may, at the taxpayer's election, be immediately deducted or capitalized and amortized. In addition, H.R.1 provides that for taxable years beginning after December 31, 2021 and before January 1, 2025, certain eligible taxpayers generally may elect to retroactively deduct expenses for research and development performed in the U.S. in such taxable years by filing amended tax returns for such taxable years, and all other taxpayers that are not eligible to make such an election and that amortized expenses for research and development performed in the U.S. in such taxable years generally may elect to accelerate and deduct the remaining unamortized amounts of such research and development expenses (i) in the first taxable year beginning after December 31, 2024, or (ii) ratably over the two-taxable year period beginning with the first taxable year beginning after December 31, 2024. In recent years, many changes have been made to applicable tax laws and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

A decline in the federal budget, changes in spending or budgetary priorities of the U.S. government, a prolonged U.S. government shutdown or delays in contract awards may significantly and adversely affect our future revenues, cash flow and financial results.

In recent years, U.S. government appropriations have been affected by larger U.S. government budgetary issues and related legislation. As a result, the Department of Defense funding levels have fluctuated and have been difficult to predict. Future spending levels are subject to a wide range of factors, including Congressional action. In addition, in the past, U.S. debt ceiling and budget deficit concerns have increased the possibility of additional credit-rating downgrades and economic slowdowns, or a recession in the U.S. Although U.S. lawmakers passed legislation to raise the federal debt ceiling on multiple occasions, ratings agencies have lowered or threatened to lower the long-term sovereign credit rating on the U.S. The impact of this or any further downgrades to the U.S. government's sovereign credit rating or its perceived creditworthiness could adversely affect the U.S. and global financial markets and economic conditions.

As a result, government spending levels are difficult to predict beyond the near term due to numerous factors, including the external threat environment, future government priorities and the state of government finances. Significant changes in government spending or changes in U.S. government priorities, policies and requirements could have a material adverse effect on our results of operations, financial condition or liquidity.

The U.S. Congress, the Trump administration, or any new administration may make substantial changes to fiscal, tax, and other federal policies that may adversely affect our business

Since the start of the Trump Administration in 2025, U.S. policy changes have been implemented at a rapid pace and additional changes are likely. Changes to U.S. policy implemented by the U.S. Congress and the current administration have impacted and may in the future impact, among other things, the U.S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U.S. regulatory environment, inflation and other areas. Although we cannot predict the impact, if any, of these changes to our business, they could adversely affect our business. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could hinder our ability to compete in certain markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

Our operations are subject to U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. Anti-corruption laws generally prohibit us and our employees, officers, CROs, consultants, contractors and other

partners and agents from authorizing, promising, offering, providing, soliciting, or receiving, directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase over time. We expect to rely on third parties for research, preclinical studies and clinical trials and/or to obtain necessary permits, licenses, patent registrations and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

We are also subject to U.S. and foreign export controls, trade sanctions, and import laws and regulations. Such laws may prevent or prohibit the export or provision of certain products and services to countries, governments, and persons targeted by sanctions. Violations of these above laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, breach of contract and fraud litigation, reputational harm and other consequences.

Risks Related to Third Party Relationships

We currently rely on, and may continue to depend on, collaborations with third parties for the discovery, development and commercialization of our product candidates. If any of these collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates.

We have a third-party collaborator for research, development and commercialization of some of our product candidates, and we may seek third-party collaborators in the future. Pharmaceutical companies are our prior and likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements. If we fail to maintain our existing collaborations or fail to enter into future collaborations on commercially reasonable terms, or at all, or if such collaborations are not successful, we may not be able to execute our strategy to develop certain targets, product candidates or disease areas that we believe could benefit from the resources of either larger pharmaceutical companies or those specialized in a particular area of relevance.

For example, in May 2025, we entered into the Collaboration Agreement with Novo. Under the Novo Collaboration Agreement, we and Novo are exclusively collaborating to leverage our proprietary Native Complex Platform® to discover, develop and commercialize multiple potential oral small molecule therapies for metabolic-related diseases based on certain specified molecular targets. The collaboration objective is to discover and develop several novel mono-, dual-, or triple-acting oral small molecule drug candidates directed across five Collaboration Targets. The collaboration includes our most advanced preclinical metabolic program focused on developing an oral small molecule agonist to the GIP receptor. We and Novo have initially commenced four simultaneous research and development programs, with each pursuing one or more Collaboration Targets from discovery through development candidate selection. Failure by Novo to meet its obligations under the Novo Collaboration Agreement, to apply sufficient efforts at developing and commercializing licensed products, or to comply with applicable legal or regulatory requirements, may materially adversely affect our business and our results of operations.

With respect to our collaboration agreements, we have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Moreover, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates may pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials 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;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- 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; and
- 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.

As a result of the foregoing, our existing collaboration or any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. If a current or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. Any failure to successfully develop or commercialize our product candidates pursuant to any current or future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Moreover, to the extent that any of our current or future collaborators were to terminate a collaboration agreement, we may be forced to independently develop these product candidates, including funding preclinical studies or clinical trials, assuming marketing and distribution costs and defending intellectual property rights, or, in certain instances, abandon product candidates altogether, any of which could result in a change to our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

We rely on third-party manufacturers, CROs, CMOs, and suppliers to supply, develop and test components of our product candidates. The loss of our third-party manufacturers, CROs, CMOs, or suppliers, their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, or changes in methods of product candidate manufacturing, development or formulation would materially and adversely affect our business.

We do not own or operate facilities for drug manufacturing, storage, distribution or quality testing. We currently rely, and may continue to rely, on third-party contract manufacturers, including in China, to manufacture and test bulk drug substances, drug products, raw materials, samples, components, or other materials and reports. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, terminated or of satisfactory quality or continue to be available at acceptable prices. In addition, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA, EMA and foreign regulatory authority review. In some cases, we, and our suppliers and manufacturers, some of which may be our sole source of supply, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA, EMA, and other comparable foreign regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA, and other comparable foreign regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of elements of our product candidates. Moreover, we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such to another third party.

These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines; and we may be required to repeat some of the development program. The delays

associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce our products will be subject to periodic review and inspection by the FDA and foreign regulatory authorities, including for continued compliance with cGMP requirements, quality control, quality assurance and corresponding maintenance of records and documents. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements, comply with cGMPs or maintain a compliance status acceptable to the FDA or foreign regulatory authorities could adversely affect our business in a number of ways, including:

- delay in the progress on certain research programs;
- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of existing or future collaborators;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our therapeutics.

Additionally, our contract manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our contract manufacturers were to encounter any of these difficulties, our ability to provide our product candidates to patients in preclinical and clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

In addition, we currently rely on foreign CROs and CMOs, including WuXi AppTec (Hong Kong) Limited, for manufacturing and development activities and will likely continue to rely on foreign CROs and CMOs in the future. Foreign CMOs may be subject to 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.

For example, the BIOSECURE Act passed in December 2025 prohibits U.S. federal agencies from entering into or renewing a contract with any company that uses biotechnology equipment or services produced or provided by a "biotechnology company of concern" in the performance of that contract. It also prohibits loans or grant funding from U.S. federal agencies to entities that use any biotechnology equipment or services produced or provided by a "biotechnology company of concern" in the performance of the government grant or loan. As the BIOSECURE Act is recently enacted, the full effects on our industry is unknown; however, it could have the downstream effect of restricting the ability of pharmaceutical companies that enter into contracts with or receive funding from U.S. federal agencies from purchasing services or equipment from certain Chinese biotechnology companies, including those that are specifically named in the proposed BIOSECURE Act, as well as supply chain disruptions or delays. As passed in December 2025, the BIOSECURE Act does not currently name WuXi Biologics or WuXi AppTec as "biotechnology companies of concern," but treats any company on the Department of Defense "1260H list" (named after Section 1260H of the NDAA for Fiscal Year 2021) of "Chinese military companies" as a "biotechnology company of concern." By December 18, 2026, the Director of the Office of Management and Budget ("OMB") will publish a full list of "biotechnology companies of concern" based on recommendations from key federal Secretaries and Directors, including Defense, Justice, HHS, Commerce, National Intelligence, Homeland Security, State, and National Cyber. The Director of OMB will thereafter review and update that list at least annually, based on recommendations from those key federal Secretaries and Directors. To the extent WuXi Biologics, WuXi AppTec or other contractors we use are named as "biotechnology companies of concern" or if we have an existing contract with a company subsequently added to the "biotechnology companies of concern," a grandfathering provision contained within the BIOSECURE Act may allow us adequate time to identify and execute agreements with alternative contractors if necessary (although there is no guarantee the terms under which we would engaged an alternative contractor would be favorable or how the government implements the BIOSECURE Act). Depending on how the BIOSECURE Act is interpreted by U.S. federal agencies, and whether the BIOSECURE Act is subsequently amended, we could be potentially restricted from pursuing U.S. federal government business or government reimbursement for our products in the future if we

continue to use WuXi Biologics, WuXi AppTec or other suppliers or partners identified as "biotechnology companies of concern" beyond this grandfathering period.

In addition to the BIOSECURE Act, any additional executive action, legislative action, or potential sanctions with China could materially impact our work with WuXi STA. U.S. executive agencies have the ability to designate entities and individuals on various governmental prohibited and restricted parties lists. Depending on the designation, potential consequences can range from a comprehensive prohibition on all transactions or dealings with designated parties, or a limited prohibition on certain types of activities, such as exports and financing activities, with designated parties.

For example, the pharmaceutical industry in China is strictly regulated by the Chinese government. Changes to Chinese regulations or government policies affecting pharmaceutical companies are unpredictable and may have a material adverse effect on our collaborators in China which could have an adverse effect on our business, financial condition, results of operations and prospects. Evolving changes in China's public health, economic, political, and social conditions and the uncertainty around China's relationship with other governments, such as the U.S. and the United Kingdom, or U.K., could also negatively impact our ability to manufacture our product candidates for our planned clinical trials or have an adverse effect on our ability to secure government funding, which could adversely affect our financial condition and cause us to delay our clinical development programs. Any of the foregoing factors could have a material adverse effect on our business, results of operations, or financial condition.

Furthermore, as product candidates progress through preclinical and clinical trials to marketing 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 yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue.

We have entered into a collaboration agreement, and may in the future enter into additional collaboration agreements and strategic alliances to maximize the potential of our structure-based drug discovery platform and product candidates, and we may not realize the anticipated benefits of such collaborations or alliances. We expect to form collaborations in the future with respect to our product candidates, but may be unable to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.

Part of our business strategy is to explore additional collaborations with third parties to further utilize our platform capabilities on additional novel GPCR targets and to leverage partners additional disease biology understanding, development and commercial expertise, regional insights or other complementary capabilities to existing or future Septerna programs. We have therefore entered into the Novo Collaboration Agreement and may form or seek further strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our structure-based drug discovery platform or our product candidates that we may develop. These transactions can entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. As a result, if we enter into acquisition or license agreements or strategic partnerships, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or other anticipated benefits that led us to enter into the arrangement.

Research and development collaborations are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration, and may not commit sufficient efforts and resources, or may misapply those efforts and resources causing delays or termination of the research;
- collaborators may not pursue development and commercialization of our structure-based drug discovery platform or collaboration product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results or changes in their strategic focus;

- collaborators may delay, provide insufficient resources to, or modify or stop clinical trials for collaboration product candidates;
- collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our products or product candidates;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause 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 and personnel to pursue further development or commercialization of our structure-based drug discovery platform or the applicable product candidates; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property.

In addition, we could face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming, expensive, and complex. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our structure-based drug discovery platform or 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 our product candidates as having the requisite potential to demonstrate their desired safety and efficacy profile. If and when we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. Our ability to 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 our technologies, product candidates and market opportunities. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under any license agreements from entering into additional agreements on certain terms or at all with other potential collaborators.

As a result of these risks, we may not be able to realize the benefit of any future collaborations or licensing agreements we may enter into. In addition, we may face regulatory obstacles in completing such transactions. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay one or more of our other development programs, delay the potential commercialization or reduce the scope of any planned sales or marketing activities for such product candidate, or increase our expenditures and undertake development, manufacturing or commercialization activities at our own expense. If we elect to increase our expenditures to fund development, manufacturing 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 structure-based drug discovery platform or product candidates or bring them to market and generate revenue.

Additionally, we may sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. If collaborations occur, these institutions often 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 other parties, 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.

Our products require specific constituents to work effectively and efficiently, and rights to those constituents are, and in the future may be, held by others. We may also seek to in-license third-party technologies to enhance our Native Complex Platform®. We may be unable to in-license any rights from constituents, methods of use, processes or other third-party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which could harm our business. 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 in order to establish or maintain our competitive position in the market. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates or our structure-based drug discovery platform could delay the development and commercialization of our product candidates in certain geographies or limit our ability to discover and develop new product candidates, which could harm our business prospects, financial condition, and results of operations.

The manufacturing of our product candidates is complex, and our third-party manufacturers may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials, our ability to obtain marketing approval, or our ability to provide patients supply of our products, if approved, could be delayed or stopped.

The process of manufacturing pharmaceuticals is complex, time-consuming, highly regulated and subject to multiple risks. Our contract manufacturers must comply with legal requirements, cGMPs and guidelines for the manufacturing of pharmaceuticals used in clinical trials and, if approved, marketed products. Our contract manufacturers may have limited experience in the manufacturing of cGMP batches.

Manufacturing pharmaceuticals is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered at our third-party manufacturers' facilities, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with cGMPs, lot consistency and timely availability of raw materials. Even if we or our future collaborators obtain regulatory approval for any of our product candidates, there is no assurance that manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and prospects.

Scaling up a pharmaceutical manufacturing process is a difficult and uncertain task, and our third-party manufacturers may not have the necessary capabilities to complete the implementation, manufacturing and development process. If we are unable to adequately validate or scale-up the manufacturing process at our current manufacturers' facilities, we will need to transfer to another manufacturer and complete the manufacturing validation process, which can be lengthy. If we are able to adequately validate and scale-up the manufacturing process for our product candidates with a contract manufacturer, we will still need to negotiate with such contract manufacturer an agreement for commercial supply and it is not certain we will be able to come to agreement on terms acceptable to us.

We cannot assure that any stability or other issues relating to the manufacture of any of our product candidates will not occur in the future. If our third-party manufacturers were to encounter any of these difficulties, our ability to provide any product candidates to patients in planned clinical trials and products to patients, once approved, would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of planned clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Any adverse developments affecting clinical or commercial manufacturing of our product candidates or products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our product candidates or products. We may also have to take inventory write-offs and incur other charges and expenses for product candidates or products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could adversely affect our business and delay or impede the development and commercialization of any of our product candidates or products, if approved, and could have an adverse effect on our business, prospects, financial condition and results of operations. Regional or single-source dependencies may in some cases accentuate these risks. For example, the pharmaceutical industry generally, and in some instances our Company, our collaborators or other third parties on which we rely, depend on China-based suppliers or service providers for certain raw materials, products and services, or other activities. Our ability or the ability of our collaborators or such other third parties to continue to engage these China-based suppliers or service providers for certain preclinical research programs and clinical development programs could be restricted due to geopolitical development between the United States and China, including as a result of the escalation of tariffs or other trade restrictions, the BIOSECURE Act or the enactment of new laws that limit our ability to freely contract for goods or services.

As part of our process development efforts, we also may make changes to the manufacturing processes at various points during development, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of our clinical trials. In some circumstances, changes in the manufacturing process may require us to perform *ex vivo* comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require

us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial.

We intend to rely on third parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We do not currently have the ability to independently conduct preclinical studies or clinical trials required to develop our product candidates. We intend to rely on CROs, clinical trial sites and other third parties to ensure the proper and timely conduct of our preclinical studies and clinical trials, and we expect to have limited influence over their actual performance. We intend to rely upon CROs and others for the execution of future nonclinical studies and to monitor, manage and report data for our clinical trials. We expect to control only certain aspects of our CROs' and others' activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies or clinical trials are conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs and others does not relieve us of our regulatory responsibilities.

We, our CROs and other third parties we might engage will be required to comply with good laboratory practices ("GLPs") and GCPs, which are regulations and guidelines enforced by the FDA, EMA, and other comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. The regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we will rely on CROs and others to conduct GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs and others does not relieve us of our regulatory responsibilities. If we, our CROs and other third parties we engage fail to comply with GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA, or other comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Accordingly, if our CROs or others fail to comply with these regulations or fail to recruit a sufficient number of participants, we may be required to repeat clinical trials, which would delay the regulatory approval process.

While we will have agreements governing their activities, our CROs and other third parties we engage will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future nonclinical and clinical programs. These CROs and others may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs and others, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. In addition, certain of our agreements with CROs and other third parties currently or will provide for monetary and other limitations on their liability. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for any other reasons, our preclinical or clinical programs may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed, decreased or eliminated.

If our relationship with these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial 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 negatively impact our ability to meet our desired development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, financial condition and prospects.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of our product candidates.

We currently depend and in the future may continue to depend on single- or limited-source suppliers for some of the components and materials used in the product candidates we may develop.

We currently depend and in the future may continue to depend on single- or limited-source suppliers for some of the components and materials used in any product candidates we may develop. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes and finished goods could expose us to several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

If we have to switch to a replacement supplier, the manufacture and delivery of any product candidates we may develop could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers, if required, may not be accomplished quickly or at all. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single source components and materials used in our therapeutics, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our product candidates.

Risks Related to Intellectual Property

If we are unable to obtain, maintain, defend and enforce patent or other intellectual property protection for our current or any future product candidates, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We anticipate that we will file additional patent applications both in the United States and in other jurisdictions, as appropriate. However, we cannot predict:

- if and when any patents will issue;
- the degree and scope of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether others will apply for or obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether we will need to initiate litigation or administrative proceedings to defend our patent rights, which may be costly whether we win or lose; or
- whether the patent applications that we own, or may in-license, will result in issued patents with claims that cover our product candidates or uses thereof in the United States or in foreign jurisdictions.

We rely, and may in the future rely, upon a combination of patent, trade secret and trademark protection for our current and any future product candidates and proprietary technologies to prevent third parties from exploiting our achievements, thus eroding our competitive position in our market. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property and proprietary information. Our success depends in large part on our ability to obtain, maintain, expand, enforce, and defend the scope, ownership or control, validity and enforceability of our intellectual property protection in the United States and other countries with respect to our current and any future product candidates and other proprietary technologies we may develop. Our commercial success depends in large part on our ability to obtain and maintain patent protection in the United States and other jurisdictions with respect to our current and any future product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our current and future development programs and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner, including as a result of factors impacting our, our licensors' or governmental patent offices' operations.

It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our current or any future product candidates in the United States or in foreign jurisdictions. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been or will be found, which unknown prior art can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do issue and even if such patents cover our current or any future product candidates, third parties may challenge their scope, validity, or enforceability, which may result in such patents being

narrowed, invalidated, or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

If the patent applications we hold or have in-licensed with respect to our product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for current or any future product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future drug products. Any such outcome could have a negative effect on our business.

Composition of matter patents for pharmaceutical products provide intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that the claims in our pending patent applications covering the composition of matter of any of our product candidates will be considered patentable by the USPTO, or by patent offices in foreign jurisdictions, or that the claims in any of our patents that may issue will be considered valid and enforceable by courts in the United States or foreign jurisdictions. Method of use patents protect the use of a product for the specified method. We cannot be certain, however, that the claims in our pending patent applications covering methods of use of our product candidates will be considered patentable by the USPTO, or by patent offices in foreign jurisdictions, or that the claims in any of our patents that may issue will be considered valid and enforceable by courts in the United States or foreign jurisdictions. Further, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, once approved for therapeutic use by FDA. or counterpart foreign regulatory authorities, physicians may prescribe these products "off-label" for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or enforce against.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. Patent applications in the United States and certain other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to file for patent protection. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies or products.

Changes in either the patent laws or interpretation of the patent laws in the United States and other jurisdictions may diminish the value of our patents or narrow the scope of our patent protection. These changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a negative effect on our business.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or another patent office or become involved in opposition, derivation, reexamination, *inter partes* review ("IPR"), post-grant review ("PGR") or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights or obtaining a costly license from a third party. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize our product candidates.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology, products or methods, or limit the duration of the patent protection of our technology, products or methods.

Moreover, patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years from the earliest filing date of a non-provisional patent application. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. For instance, a patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not necessarily extend to all claims, but instead only to claims that read on the product as approved. Laws governing analogous patent term

extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. In addition, although upon issuance in the United States a patent's term can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. Without patent protection for our product candidates, including once the patent life has expired even if patents covering our product candidates are obtained, we may be open to competition from generic versions of such drugs. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent term has expired for a product, we may be open to competition from generic medications. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

Even if we have or obtain patents covering our products or methods, we may still be barred from making, using and selling such products or methods because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering compositions, products or methods that are similar or identical to ours, which could materially affect our ability to successfully develop our technology or to successfully commercialize any approved products alone or with collaborators.

Patent applications in the United States and elsewhere are generally published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our methods and product candidates could have been filed by others without our knowledge. Additionally, pending claims in patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies or related products. These patent applications may have priority over patent applications filed by us.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor, co-inventor, owner or co-owner. For example, we or our licensors may have inventorship or ownership disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, we may be required to pay monetary damages and we may also lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may allege that we have infringed or misappropriated their intellectual property. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. 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 market 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our

product candidates. We cannot be certain that our product candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties. Third parties may assert infringement claims against us based on existing or future intellectual property rights. In the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our investigational products or force us to cease some of our business operations, which could materially harm our business.

We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our product candidates, might assert are infringed by our product candidates, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates and other proprietary technologies we may develop, could be found to be infringed by one or more of our product candidates. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. The pharmaceutical and biotechnology industries have produced a considerable number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products 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. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents, and there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. 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, which could have a material adverse effect on our business and operations. 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 litigation. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

We may choose to challenge the enforceability or validity of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in an *ex parte* re-examination, IPR or PGR proceeding. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office ("EPO"), or other foreign patent office. The costs of these opposition proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office, then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

If we are found to infringe a third-party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, and could divert the time and attention of our technical personnel and management, cause development delays, and/or require us to develop non-infringing technology, which may not be possible on a cost-effective basis, any of which could materially harm our business. In the event of a successful claim of infringement against us, we may have to pay substantial monetary damages, including treble damages and attorneys' fees for willful infringement, pay royalties and other fees, redesign our infringing drug or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Our technology licensed from various third parties may be subject to retained rights.

Our future licensors may retain certain rights under the relevant agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act ("Bayh-Dole Act"). The federal government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights." March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants." If the patent owner refuses to do so, the government may grant the license itself. We sometimes collaborate with academic institutions to accelerate our preclinical research or development, creating a risk that federal funds may be commingled. Therefore, we cannot be sure that any intellectual property co-developed from a collaboration with an academic institution will be free from government rights pursuant to the Bayh-Dole Act. If, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration date of a third-party patent, which might adversely affect our ability to develop and market our products.

We may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our product candidates. Thus, we cannot guarantee that our product candidates, or our commercialization thereof, do not and will not infringe any third party's intellectual property.

We cannot guarantee that any patent searches or analyses that are performed, including the identification of relevant patents, the scope of patent claims or the expiration dates of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. The scope of a patent claim is 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 future products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our future products.

One aspect of the determination of patentability of our inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim.

The landscape of intellectual property related to our product candidates and future products is constantly changing. Therefore, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates or their intended uses, and as a result the impact of such third-party intellectual property rights upon the patentability of our own patents and patent applications, as well as the impact of such third-party intellectual property upon our freedom to operate, is highly uncertain. Because patent applications in the United States and certain other jurisdictions are confidential for typically a period of at least 18 months after their priority date, or may not be published at all, we cannot be certain that we were the first to file any patent application related to our product candidates. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Furthermore, for U.S. applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. For U.S. applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law in view of the passage of the America Invents Act, which brought into effect significant changes to the U.S. patent laws, including new procedures for challenging pending patent applications and issued patents. Should we fail to win an interference challenge, a third party may obtain rights to intellectual property related to our product candidates and future products.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

Because our programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue 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, capital 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. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents and patent applications relating to our product candidates are controlled by our future licensors or collaboration partners. If any of our future licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

We may enter into license agreements in the future with others to advance our existing or future research or allow commercialization of our product candidates. These licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology platform or product candidates in the future.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. In such an event, 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 future licensors fail to prosecute, maintain, enforce, and defend such patents or patent applications, 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 product candidates that are subject of such licensed rights could be adversely affected.

Our future licensors may rely on third-party consultants or collaborators or on funds from third parties such that our future licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights to our future in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

It is possible that we may be unable to obtain necessary licenses at a reasonable cost or on reasonable terms, if at all. 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 (which could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects). In the event we are unable to obtain necessary licenses at a reasonable cost or on reasonable terms, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

Disputes may arise between us and our future 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 patents and other rights to third parties;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology from third parties are 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 increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we license in the future prevent or impair our ability to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our future licensors might conclude that we materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

From time to time, we may be required to license technologies relating to our programs from additional third parties to further develop or commercialize our product candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our product candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our product candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or license is not valid, is unenforceable and/or is not infringed. If we or our current or future collaborators were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including but not limited to lack of novelty, obviousness, or insufficient written description or enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, interference proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in loss of rights to, the revocation of, cancellation of or amendment to our patents in such a way that they no longer cover our technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a patent claim. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates or other intellectual property that we may develop. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened or questioned,

it could dissuade companies from collaborating with us to license, develop or commercialize our product candidates. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights 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 or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. 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 conduct such litigation or proceedings adequately. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including confidential information, know-how or trade secrets, of a third-party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors 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 we have wrongfully hired an employee from a competitor or that we or these employees, consultants or contractors have used or disclosed such third-party intellectual property, including know-how, trade secrets or other proprietary information, to us. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, it may a have negative impact on our business and our ability to develop product candidates or commercialize our technology. In addition to paying substantial monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could incur substantial costs and be a distraction to management and scientific personnel.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

We may license intellectual property rights from third parties. Such licenses may be subject to early termination if we fail to comply with our obligations in our licenses with third parties, which could result in the loss of rights or technology that are material to our business.

We may become a party to licenses that give us rights to third-party intellectual property or technology that is necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements, we are or may become obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. These fees may be significant, which could make it difficult for us to achieve or maintain profitability. In addition, under certain of such agreements, we are or may become required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations, including due to our use of the intellectual property licensed to us in an unauthorized manner, and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business, harming our ability to develop, manufacture and/or commercialize our platform, products or product candidates.

In addition, the agreements under which we license intellectual property or technology to or from third-parties can be 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 increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. The failure to obtain or in-license any compositions, methods of use, processes or other third-party intellectual property rights at a reasonable cost or on reasonable terms, could harm our business. If we fail to obtain licenses to necessary third-party intellectual property rights, we may need to cease use of the compositions or methods covered by such third-party intellectual property rights. Furthermore, we may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. 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.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned and licensed patents and/or applications and any patent rights we may own or license in the future. We rely on our outside counsel, patent annuity service providers, or our licensing partners to pay these fees to the applicable government patent agencies. If these fees are not paid when due, our rights to such patents or patent applications may be irrevocably abandoned or otherwise materially impaired.

The USPTO and various non-U.S. government patent agencies require compliance with numerous procedural, documentary, and other similar provisions during the patent application process. For example, many jurisdictions, including the U.S. and China, require a foreign filing license before seeking patent protection in a jurisdiction outside of the jurisdiction of which the inventor is a citizen or in which the invention was made. Each jurisdiction's laws regarding foreign filing licenses vary and may even conflict. We employ reputable law firms in foreign jurisdictions and other professionals to help us comply and we are also dependent on any licensors to take the necessary action to comply with these requirements with respect to our intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance 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.

Additional non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting, maintaining, enforcing, and defending patent applications and patents covering our current and any future product candidates worldwide is prohibitively expensive, so we will pursue patents in a limited number of jurisdictions. Moreover, our intellectual property rights in some jurisdictions outside the United States can have a different scope and strength than do those in the United States. Consequently, we will not be able to prevent third parties from practicing our inventions in all jurisdictions, or from selling or importing in and into various jurisdictions products made using our inventions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own product candidates and, further, may export otherwise infringing product candidates to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. Further, these product candidates may compete with our product candidates in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems protecting and defending intellectual property rights in jurisdictions outside the United States. The legal systems of certain jurisdictions do not favor the enforcement of patents, trade secrets and other intellectual property rights, particularly those relating to pharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, including the marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patents and other intellectual property rights in jurisdictions outside the United States could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly,

could put our patent applications at risk of not issuing, and could provoke third parties to assert claims of infringement or misappropriation 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. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business.

Our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in intellectual property laws in the United States and around the world. For example, in Europe, a new unitary patent system took effect June 1, 2023, which will significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court ("UPC"). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes. Certain jurisdictions, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties under certain circumstances. In those jurisdictions, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. In addition, many jurisdictions limit the enforceability of patents against government agencies or government contractors. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop and our technology, one or more U.S. patents that we license or may own in the future may be eligible for limited patent term extension under the Hatch-Waxman Amendments. Under certain circumstances the Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought and within 60 days of FDA approval. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable patent term extension or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or the term of any such extension is less than we request, we may be open earlier than projected to competition from competitive products, including generics or biosimilars following our patent expiration, and our revenue could be reduced earlier than projected. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of our trade secrets and other proprietary information. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary information and confidential know-how that we elect not to patent, including processes for which patents are difficult to enforce, and any other elements of our product candidates, technology and product discovery, development processes and drug discovery platform that involve proprietary know-how, information, or technology that is not covered by patents. In particular, our trade secrets, confidential know-how and other proprietary information includes our proprietary Native Complex Platform® drug discovery platform, which we do not plan to patent. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Such risk of disclosure can be increased by our use of AI technologies and can result in misappropriation and other security incidents. Because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Trade secrets, confidential know-how and proprietary information, however, may be difficult to protect. We seek to protect our trade secrets, confidential know-how and proprietary information, including our proprietary processes and drug discovery platform, in part, by entering into confidentiality agreements with our employees, consultants, outside scientific advisors, contractors, and collaborators. With our consultants, contractors, and outside scientific collaborators, these agreements typically include invention assignment obligations. Although we use reasonable efforts to protect our trade secrets, we cannot provide any assurances that all such agreements have been duly executed, and notwithstanding the existence of a confidentiality agreement our employees, consultants, outside scientific advisors, contractors, and collaborators might intentionally or inadvertently disclose our trade secret information, including to competitors. In addition, competitors or other third parties may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Despite our efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. Furthermore, the laws of some foreign jurisdictions do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition. Further, although we maintain cyber liability insurance, this insurance may not provide adequate coverage against potential liabilities related to any experienced cybersecurity incident or data breach.

Our intellectual property rights do not necessarily protect against all potential threats to our business.

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. These risks and uncertainties include the following:

- others may be able to make compounds or formulations that are similar to our product candidates but that are not covered by the claims of any patents, should they issue, that we own or control;
- we or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or control;
- we might not have been the first to file patent applications covering certain of our product candidates or inventions we own or control;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- pending patent applications that we own or control may not lead to issued patents;
- issued patents that we own or control may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other jurisdictions that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in jurisdictions where we do not have patent rights and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Our current or future trademarks or trade names may be challenged, opposed, infringed, circumvented, invalidated, cancelled, declared generic, determined to be not entitled to registration, or determined to be infringing on other marks. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many other jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Trademark litigation could be expensive. In addition, we could be found liable for significant monetary damages, including treble damages, disgorgement of profits and attorneys' fees, if we are found to have willfully infringed a trademark. We may not be able to protect our exclusive right to trademarks or trade names or may be forced to stop using these names,

which we need for name recognition by potential collaborators or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks or trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks or trade names to third parties, such as distributors. Though these agreements may provide guidelines for how our trademarks or trade names may be used, a breach of these agreements or misuse of our trademarks or tradenames by third parties may jeopardize our rights in or diminish the goodwill associated with our trademarks or trade names.

Moreover, any name we have proposed to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA or equivalent body. Furthermore, in many jurisdictions, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties 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 that incorporate variations of our registered or unregistered trademarks or trade names. Furthermore, assertions of potential trademark infringement or possible market confusion may lead to coexistence agreements in order to avoid costly disputes related to our trademarks. As a consequence, we may be forced to amend the list of goods and services covered by our trademarks more narrowly than as originally filed and intended, which could adversely affect our ability to establish name recognition. 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. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain name or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Rights to improvements to our product candidates may be held by third parties.

In the course of testing our product candidates, we may enter into agreements with third parties to conduct clinical testing, which may provide that improvements to our product candidates may be owned solely by a third party or jointly between the parties. If we determine that rights to such improvements owned solely by a third party are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain a license from such third party in order to use the improvements and continue developing, manufacturing or marketing the product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby giving our competitors and other third parties access to the same technologies licensed to us. Failure to obtain a license on commercially reasonable terms or at all, or to obtain an exclusive license, could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. If we determine that rights to improvements jointly owned between us and a third party are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain an exclusive license from such third party. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such improvements, such co-owners may be able to license their rights to other parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our intellectual property in order to enforce such intellectual property against other parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Risks Related to Ownership of Our Common Stock

We do not know whether a market will be sustained for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Although our common stock is listed on the Nasdaq Global Market ("Nasdaq"), an active trading market for our common stock may not be sustained. If a market for our common stock is not sustained or if trading volume in our common stock is low, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares.

The market price for our common stock may be influenced by those factors discussed in this "Risk Factors" section and many others, some of which may include:

- the success of existing or new competitive product candidates or technologies;
- the commencement, enrollment, completion and results of preclinical studies and clinical trials for our product candidates;
- adverse results or delays, suspensions or terminations in future preclinical studies or clinical trials;
- unanticipated serious safety concerns related to our product candidates;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates or the failure of a regulatory authority to accept data from preclinical studies or clinical trials conducted in other countries;
- failure to commercialize our product candidates, if approved;
- failure or discontinuation of any of our development and research programs;
- results of any preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs or product candidates that we may develop;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, if any, that cover our stock;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- expiration of market stand-off or lock-up agreements;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- trading volume of our common stock;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general, and the market for pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad

market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources.

Future sales, or the perception of future sales, of our common stock in the public market by existing stockholders could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

As of December 31, 2025, we had 44,806,272 shares of our common stock outstanding. Shares of unvested restricted stock that were issued and outstanding will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market stand-off or lock-up agreements. Shares issued upon the exercise of stock options pursuant to future awards that may be granted under our equity incentive or inducement plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements and Rule 144 and Rule 701 under the Securities Act.

Certain holders of our common stock have rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have registered the offer and sale of all shares of common stock that we may issue under our equity compensation plans, and those shares are available for sale in the open market, unless such shares are subject to vesting restrictions with us or any applicable lock-up restrictions. Once we register the offer and sale of shares for the holders of registration rights, they can be freely sold in the public market upon issuance, subject to any applicable lock-up agreements.

In addition, we expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, in the future, we may issue additional shares of our common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

We are an "emerging growth company" and a "smaller reporting company," and the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may 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 may 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 of 2022 ("Sarbanes-Oxley Act"), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the completion of our initial public offering ("IPO"), although circumstances could cause us to lose that status earlier, including if we are deemed to be a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30, or if we have total annual gross revenue of $1.235 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act;
- not being required to comply with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on the financial statements.
- reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

In addition, the JOBS Act provides that an emerging growth company can also take advantage of an extended transition period for complying with new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards, and therefore, while we are an emerging growth company, we will not be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company" as defined in the Exchange Act, and we may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. We may continue to be a smaller reporting company even after we are no longer an emerging growth company, which would allow us to take advantage of many of the same exemptions from disclosure requirements and reduced disclosure obligations regarding executive compensation in this Annual Report and our periodic reports and proxy statements. 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 share price may be more volatile.

We have incurred and will continue to incur significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company, and these expenses may increase even more after we are no longer an "emerging growth company." We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial reporting controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act ("Dodd-Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to the fifth anniversary of our IPO. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have an adverse effect on our business. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Insiders have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.

Based on the beneficial ownership of our common stock as of December 31, 2025, our directors and executive officers, holders of 5% or more of our capital stock and their respective affiliates beneficially own a significant percentage of our outstanding common stock. These stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

We do not expect to pay any dividends for the foreseeable future. Investors may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We have never declared or paid cash dividends on shares of our common stock and do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock.

Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

If we fail to maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles in the United States ("U.S. GAAP"). As a public company, we are required to incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, beginning with our second Annual Report on Form 10-K after we become a public company, we are required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company, we may be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. We are engaged in the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy or consequent inability to produce accurate financial statements on a timely basis could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis cause investors to lose confidence in the accuracy and completeness of our financial reports and could cause the market price of our common stock to decline significantly.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If we experience material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

We may in the future discover material weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline, and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our amended and restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed only for cause;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorized our board of directors to make, alter, amend or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock.

In addition, because we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

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

Our amended and restated bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by 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 bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of, or a claim based on, fiduciary duty owed by any of our current or former directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is governed by the internal affairs doctrine ("Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act ("Federal Forum Provision"). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our

directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court and other state courts have upheld the validity of federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

General Risk Factors

Unfavorable global economic conditions, political instability and geopolitical events could adversely affect our business, financial condition, stock price, and results of operations.

Our business could be adversely affected by unstable economic and political conditions within the United States and foreign jurisdictions, including as a result of an economic downturn and geopolitical events, such as changes in or disruptions of U.S. governmental agencies, whether from a prolonged U.S. federal government shutdown or reduced resources, disruptions in capital markets, the potential for significant changes in U.S. federal policies or regulatory environment or other factors that affect the geopolitical landscape. The global credit and financial markets have also generally experienced extreme volatility and disruptions (including as a result of actual or perceived changes in interest rates, inflation and macroeconomic uncertainties), which has included severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, high inflation, changes in interest rates, uncertainty about economic stability, global supply chain disruptions, and increases in unemployment rates. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A severe or prolonged economic downturn could result in a variety of risks to our business, including a decrease in the demand for our product candidates and in our ability to raise additional capital when needed on acceptable terms, if at all.

The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflicts, such as the ongoing conflicts between Russia and Ukraine, and Israel and Hamas, terrorism, or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also continue to adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. Additionally, changes to policy implemented by the U.S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U.S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U.S. regulatory environment, inflation and other areas. For example, the implementation of tariffs by the U.S. government has led to increased trade and political tensions, between not only the U.S. and China, but also between the U.S. and other countries in the international community. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. For example, the BIOSECURE Act signed into law as part of the recently-enacted NDAA may restrict the ability of United States pharmaceutical companies to purchase services or products from, or otherwise collaborate with, certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise receive funding from, the United States government. We continue to assess the legislation as it develops to determine whether it could have an effect on our contractual relationships. Any changes in political, trade, regulatory, and economic conditions, including U.S. trade policies, could have a material adverse effect on our financial condition or results of operations. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.

Furthermore, any disruptions to our supply chain as a result of unfavorable global economic conditions, including due to geopolitical conflicts or public health crises, could negatively impact the timely execution of our ongoing and future clinical trials. In addition, current inflationary trends in the global economy may impact salaries and wages, costs of goods and transportation expenses, among other things, and recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures may create market and economic instability. We cannot anticipate all of the ways in which the foregoing, and the current economic climate and financial market conditions generally, could adversely impact our business.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and our financial condition and results of operations.

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.

Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect our Company, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- potential or actual breach of statutory, regulatory or contractual obligations, including obligations that require us to maintain letters of credit or other credit support arrangements;
- termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the United States or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity, our current and/or planned business operations, and our current or projected financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our suppliers, which in turn, could have a material adverse effect on our current and/or planned business operations and our current or projected results of operations and financial condition. For example, a customer may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition, a customer or supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that could result in material adverse impacts on the Company, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. Any customer, collaborator or supplier bankruptcy or insolvency, or the failure of any customer or collaborator to make payments when due, or any breach or default by a customer, collaborator or supplier, or the loss of any significant supplier or collaborator relationships, could result in material losses to the Company and may have a material adverse impact on our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will depend in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock or publishes inaccurate or unfavorable research bout our business, the price of our stock could decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

We may become involved in litigation and investigations that could divert management's attention and harm our business, and insurance coverage may not be sufficient to cover all costs and damages.

From time to time we may be subject to litigation claims and investigations from the SEC and other government agencies through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal data, government-issued subpoenas, contractual relations with collaborators and licensors and intellectual

property rights. In the past, securities class action litigation has often followed certain significant business transactions, such as the sale of a company or announcement of any other strategic transaction, the announcement of negative events, such as negative results from clinical trials, or periods of volatility in the market price of a company's securities. These events may also result in or be concurrent with investigations by the SEC (which may not be publicly disclosed by the SEC or by us, particularly where the SEC or investigating body has made it clear that no wrongdoing has been alleged). In addition, we may be exposed to litigation or investigation even if no wrongdoing has occurred. Responding to litigations and investigations is usually expensive, and our insurance coverage many not be sufficient to cover the legal costs for doing so, as well as any damages for which we are ultimately held responsible. In addition, responding to a litigation or an investigation diverts management's attention and resources, which could adversely affect our business and cash resources and our ability to consummate a potential strategic transaction or the ultimate value our stockholders receive in any such transaction.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

While we maintain commercial insurance at a level we believe is appropriate against certain risks commonly insured in the industry in which we operate, there is no guarantee that our insurer will cover costs or that we will be able to obtain the desired level of coverage on acceptable terms in the future. Some of the policies we currently maintain include property, general liability, crime insurance, workers' compensation, and directors' and officers', employment practices and fiduciary liability insurance, clinical trial insurance, transportation insurance and umbrella insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Changes in the market conditions and our business operations may necessitate the addition of new insurance policies or change of our existing insurance policies. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

Our operations are vulnerable to interruption by disasters, terrorist activity, pandemics and other events beyond our control, which could harm our business.

Our facilities are located in California. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, power loss, terrorist activity, pandemics or other regional or global disasters and generally do not have a recovery plan for such events. 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.

Increased attention to, and evolving expectations for, environmental, social, and governance initiatives could increase our costs, harm our reputation, or otherwise adversely impact our business.

Companies across industries are facing increasing scrutiny from a variety of stakeholders related to their environmental, climate change, social, and governance ("ESG") and sustainability practices. Investor advocacy groups, certain institutional investors, investment funds, and other influential investors have increasingly focused on ESG practices and have placed increasing importance on the non-financial impacts of their investments. Expectations regarding voluntary ESG initiatives and disclosures may result in increased costs (including but not limited to increased costs related to compliance, stakeholder engagement, contracting and insurance), enhanced compliance or disclosure obligations, or other adverse impacts to our business, financial condition, or results of operations.

While we may at times engage in voluntary initiatives (such as voluntary disclosures, certifications, or goals, among others) to improve the ESG profile of the Company, such initiatives may be costly and may not have the desired effect. Moreover, we may not be able to successfully complete such initiatives due to factors that are within or outside of our control. Even if this is not the case, our actions may subsequently be determined to be insufficient by various stakeholders, and we may be subject to investor or regulator engagement on our ESG efforts, even if such initiatives are currently voluntary.

Certain market participants, including major institutional investors and capital providers, use third-party benchmarks and scores to assess companies' ESG profiles in making investment or voting decisions. Unfavorable ESG ratings could lead to increased negative investor sentiment towards us, which could negatively impact our share price as well as our access to and cost of capital. In addition, in recent years "anti-ESG" sentiment has gained momentum across the United States, with several states and Congress having proposed or enacted "anti-ESG" policies, legislation, or initiatives or issued related legal opinions, and the President having issued an executive order opposing diversity equity and inclusion ("DEI") initiatives in the private sector. Such anti-ESG and anti-DEI-related policies, legislation, initiatives, litigation, legal opinions, and scrutiny could result in us facing additional compliance obligations, becoming the subject of investigations and enforcement actions, or sustaining reputational harm. Therefore, to the extent we take actions that are seen as positive to some investors, other investors may take issue with such actions or face regulatory pressure to refrain from investing in, or divest from, our business. To the extent ESG matters negatively impact our reputation, it may also impede our ability to compete as effectively to attract and retain employees, which may adversely impact our operations.

In addition, we expect there will likely be increasing levels of regulation, disclosure-related and otherwise, with respect to ESG matters. For example, the SEC has issued rules that require companies to provide significantly expanded climate-related disclosures in their periodic reporting. The new climate disclosure rules were the subject of multiple legal challenges, and the SEC voluntarily stayed the climate disclosure rules pending the completion of judicial review. Therefore, it is unknown whether the new rules will go into effect and if they do, whether there will be significant changes. If the new rules go into effect and are not substantially different than the rules adopted by the SEC, we may be required to incur significant additional costs to comply, including the implementation of significant additional internal controls processes and procedures regarding matters that have not been subject to such controls in the past, and impose increased oversight obligations on our management and board of directors. Even if the SEC rules are not adopted, states or ex-U.S. jurisdictions in which we currently or may in the future operate may also have or adopt ESG or climate-related disclosure rules requiring similar or broader disclosure obligations. These and other changes in stakeholder expectations will likely lead to increased costs as well as scrutiny that could heighten all of the risks identified in this risk factor. Additionally, our business partners may be subject to similar expectations, which may augment or create additional risks, including risks that may not be known to us.

The increasing use of social media platforms presents risks and challenges.

We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally. Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates, operations, or business may cause us to be found in violation of applicable legal or contractual requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our social media policy or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, or result in public exposure of personal information of our employees, clinical trial patients, collaboration partners, and others, and which could have an adverse effect on our business, financial conditions and results of operations. Furthermore, negative posts or comments about us or our product candidates in social media could seriously damage our reputation, brand image and goodwill.

In addition, it is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to our product candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed.

Item 1B. Unresolved Staff Comments.

None

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have implemented a cybersecurity risk management program in accordance with our risk profile and business size that is informed by recognized industry standards, including elements of the National Institute of Standards and Technology Cybersecurity Framework and International Organization for Standardization 27001 Framework.

Our cybersecurity risk management program is comprised of a number of components, including but not limited to written information security policies, external cybersecurity risk assessments, and system monitoring. We also have an employee privacy and data security training awareness program that includes cybersecurity risk awareness trainings and phishing campaigns. We maintain an incident response plan to help guide our response to cybersecurity incidents.

We leverage the cybersecurity services of third-party vendors, including a third-party managed services provider and IT consultants, to support our cybersecurity risk management program and assist us in conducting external cybersecurity risk assessments. As part of our cybersecurity risk management program, we take a risk-based approach to the evaluation of third-party vendors. As part of our vendor diligence process we require vendors with access to our information technology systems and infrastructure to complete information security program questionnaires.

We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition. However, like other companies in our industry, we and our third-party vendors have from time to time experienced threats relating to our and our third-party vendors' information systems and infrastructure. For more information, please see "Item 1A, Risk Factors."

Governance Related to Cybersecurity Risks

Our board of directors has delegated cybersecurity risk management to our Audit Committee as part of the Audit Committee's general risk oversight function. The Audit Committee, through the oversight of the General Administrative Leadership team, is responsible for overseeing the Company's cybersecurity risk management processes, including oversight of mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by our General Administrative Leadership team, which consists of our CEO, CFO, COO, CPO, CLO, Vice President of Finance and Business, Vice President of Technology and our Head of Information Technology ("IT"), and is responsible for the strategic leadership of our cybersecurity risk management program. Our Head of IT, who also serves as our Information Security Officer, is responsible for the day-to-day management of our cybersecurity risk management program. The individual who is currently in this role has over thirty years of experience in information technology and cybersecurity risk management. Our Head of IT relies on both internal and external cybersecurity resources to manage and remain appraised of overall cybersecurity risks to our business and our industry.

The General Administrative Leadership team provides regular briefings regarding cybersecurity risk and related matters to our Audit Committee. Such briefings may include a discussion of cybersecurity risks and applicable risk assessments, key updates regarding our cyber strategy and related initiatives, and the emerging cybersecurity threats that may impact our business. We also provided the full board of directors with updates on matters relating to cybersecurity risk management, as necessary.

Item 2. Properties.

Our corporate headquarters are located in South San Francisco, California, where we lease and occupy approximately 44,819 square feet of combined office, research and laboratory space at 250 East Grand Avenue, South San Francisco, California 94080. The current term of our lease expires in July 2032.

We believe that our existing facilities are adequate for our current needs and for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

Item 3. Legal Proceedings.

From time to time, we may become involved in or be subject to legal proceedings, claims and litigation arising from the ordinary course of business. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

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

Our common stock began trading on the Nasdaq Global Market under the symbol "SEPN" on October 25, 2024. Prior to this date, there was no public trading market for our common stock.

Common Stock Holders

As of March 2, 2026, we had approximately 60 holders of record of our common stock. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in "street name" or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

Dividends

We have not declared or paid cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to applicable laws, and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant. In addition, our ability to pay cash dividends on our capital stock in the future may be limited by the terms of any future debt or preferred securities we issue or any credit facilities we enter into.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about securities authorized for issuance under our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report on Form 10-K (this "Annual Report").

Use of Proceeds from our IPO

On October 24, 2024, our Registration Statement on Form S-1 (File No. 333-282469), as amended, relating to our IPO was declared effective by the Securities and Exchange Commission (the "SEC") (the "Registration Statement"). Pursuant to the Registration Statement, we registered the offer and sale of 18,400,000 shares of our common stock. On October 28, 2024, we closed our IPO, pursuant to which we issued and sold 18.4 million shares of common stock at the public offering price of $18.00 per share, which included 2.4 million shares of our common stock issued and sold on October 30, 2024 to the underwriters pursuant to the full exercise of their option to purchase additional shares of our common stock, at the public offering price of $18.00 per share. Pursuant to the IPO, we received gross proceeds of $331.2 million, which resulted in net proceeds to us of $302.8 million, after deducting underwriting discounts and commissions and other offering costs payable by us of $28.4 million. J.P. Morgan Securities LLC, TD Securities (USA) LLC, Cantor Fitzgerald & Co. and Wells Fargo Securities, LLC acted as joint book-running managers for the IPO.

The net proceeds from our IPO have been invested according to our approved investment policy in a mix of money market funds and high-quality, fixed income securities. Our planned use of the net proceeds from the IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended (the "Securities Act") on October 25, 2024 has changed due to the discontinuation of the development of our prior lead product candidate, SEP-786. As a result, we currently expect to use our cash, cash equivalents and marketable securities, which include the net proceeds from the IPO, to advance SEP-479 and SEP-631 in clinical development, continue to advance the other programs in our pipeline, and the remainder to fund working capital and other general corporate purposes.

Recent Sales of Unregistered Securities

Series B Convertible Preferred Stock Financing

During the year ended December 31, 2024, we sold an aggregate of 60,828,732 shares of our Series B convertible preferred stock, at a purchase price of $1.23297 per share, for an aggregate amount of $75 million. We incurred $0.1 million in issuance costs.

No underwriters were involved in the foregoing sale of securities. The sale of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us, in connection with their purchase, that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

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.

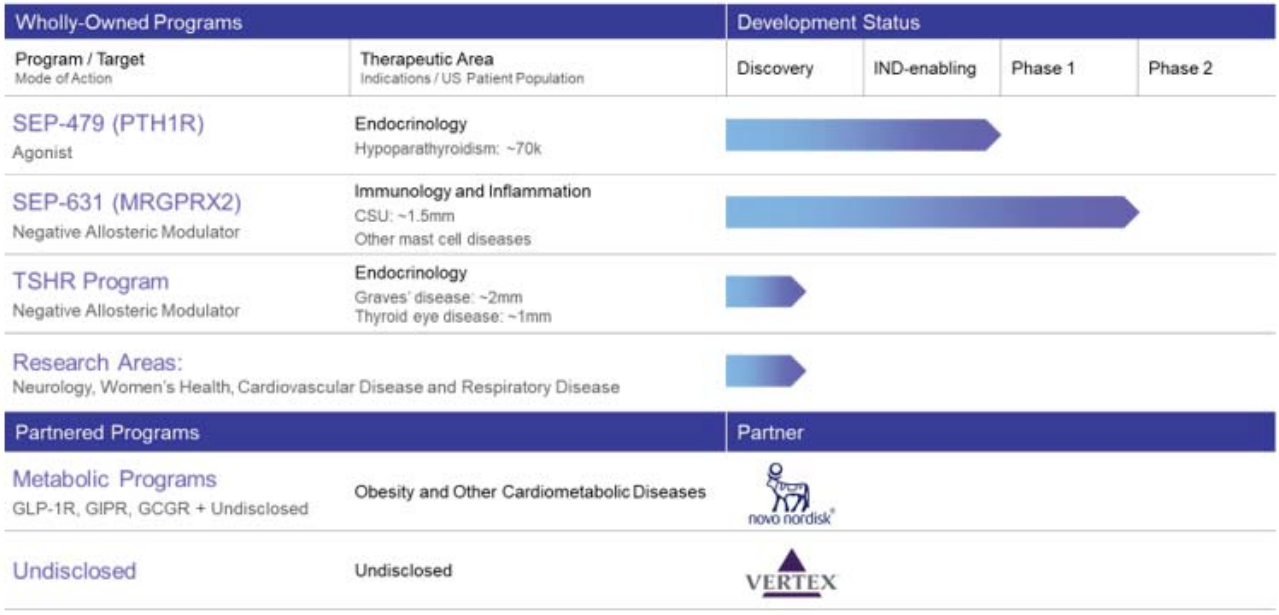
You should read the following discussion and analysis of our financial condition and results of operations together with our audited financial statements and related notes included elsewhere in this Annual Report. This discussion and other parts of this Annual Report contain forward-looking statements based upon current beliefs, plans, and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements of our plans, objectives, expectations, intentions, forecasts and projections. Our actual results and the timing of selected events could differ materially from those discussed in these forward-looking statements as a result of several factors including, but not limited to, those set forth under the section titled "Risk Factors" and elsewhere in this Annual Report. Our historical results are not necessarily indicative of the results that may be expected for any period in the future, and you should carefully read the section titled "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biotechnology company pioneering a new era of GPCR oral small molecule drug discovered powered by our proprietary Native Complex Platform®. Our industrial-scale platform aims to unlock the full potential of GPCR therapies and has led to the discovery and development of our deep pipeline of drug candidates focused initially on treating patients in three therapeutic areas: endocrinology, immunology and inflammation, and metabolic diseases.

Our proprietary Native Complex Platform® replicates the natural structure, function, and dynamics of GPCRs outside of cells at an industrial scale for, as we believe it, the first time. Our foundational technologies enable us to isolate, purify, and reconstitute full-length, properly folded GPCR proteins within ternary complexes with ligands and transducer proteins in a lipid bilayer that mimics the cell membrane. We then apply state-of-the-art discovery tools and technologies to these defined and tunable protein complexes to structurally design, screen for, and optimize potential product candidates. Leveraging our platform, we conduct GPCR oral small molecule drug discovery using an industrialized and iterative structure-based drug design approach for a diverse collection of GPCR targets. Our Native Complex Platform® is designed to enable us to target specific GPCRs, uncover novel binding pockets for validated receptors, and pursue a wide spectrum of pharmacologies, including agonists (which activate GPCR signaling), antagonists (which inhibit GPCR signaling), and allosteric modulators (which either increase or decrease the degree of GPCR activation by endogenous ligands), to affect GPCR signaling in different ways to achieve desired therapeutic effects.

We are advancing a deep portfolio of oral small molecule GPCR-targeted programs with novel mechanistic approaches to treat diseases across multiple therapeutic areas for patients with significant unmet needs. Our wholly-owned pipeline is summarized in the figure below.



Financial Overview

We were incorporated in Delaware in December 2019 under the name GPCR NewCo, Inc. In June 2021, we changed our name to Septerna, Inc. We are headquartered in South San Francisco, California.

We have incurred significant operating losses since our inception, except for the year ended December 31, 2023. Our revenue to date has been generated solely from research services. Since our founding, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, developing our proprietary and structure-based drug discovery platform, identifying and discovering our product candidates, establishing our intellectual property portfolio, conducting research and preclinical studies, including investigational new drug("IND")-enabling studies, initiating and conducting clinical trials, establishing arrangements with third parties for the manufacture of our product candidates and related raw materials, and providing general and administrative support for these operations. We have not had any products approved for sale and have not generated any revenue from product sales. Further, we do not expect to generate revenue from commercial product sales until such time, if ever, that we are able to successfully complete the development and obtain marketing approval for one or more of our product candidates. Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates.

Our net loss was $48.9 million for the year ended December 31, 2025 compared to net loss of $71.8 million for the year ended December 31, 2024. As of December 31, 2025, we had an accumulated deficit of $167.3 million. We have incurred net losses in each year since inception, except for the year ended December 31, 2023. We expect to continue to incur net losses for the foreseeable future. Our net losses may fluctuate significantly from period to period, depending on the timing and expenditures of our operational activities.

We expect to continue to incur significant and increasing net operating losses for the next several years as we:

- continue to advance our product candidates through preclinical studies and into clinical trials;
- attract, hire and retain additional personnel;
- continue to operate as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of any national securities exchange on which our securities are traded, legal, auditing, insurance expenses, investor relations activities, and other administrative and professional services;
- continue our research and development efforts and expand our pipeline of product candidates;
- acquire, discover, validate, and develop additional product candidates;
- manufacture supplies for our preclinical studies and clinical trials;
- obtain, maintain, expand, and protect our intellectual property portfolio;
- implement operational, financial and information management systems;
- make royalty, milestone or other payments under any future, license or collaboration agreements;
- potentially seek to identify, assess, acquire, or in-license or develop new technologies or additional product candidates;
- potentially experience any delays, challenges, or other issues associated with the clinical development of our product candidates, including with respect to our regulatory strategies;
- pursue regulatory approval of product candidates that successfully complete clinical trials; and
- establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval and related commercial manufacturing build-out.

Our net losses may fluctuate significantly from period to period, depending upon the timing of our expenditures on research and development activities. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our accounts payable and accrued expenses and other current liabilities, which includes accrued research and development, in the statements of cash flows in our audited financial statements included elsewhere in this Annual Report.

As a result, we will require substantial additional funding to further develop our product candidates and support our continuing operations. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. See the section titled "Liquidity and Capital Resources - Future Funding Requirements" below for additional information.

We historically financed our operations primarily through the issuances of convertible promissory notes and convertible preferred stock, an initial public offering ("IPO"), and collaborations with other companies. In October 2024, we completed our IPO, pursuant to which we issued and sold an aggregate of 18.4 million shares of our common stock (inclusive of an additional 2.4 million shares of our common stock issued and sold pursuant to the underwriters' exercise of their option to purchase additional shares in full). The aggregate net proceeds received by us from the IPO was $302.8 million, net of total offering costs of $28.4 million. In July 2025, upon the effectiveness of our Novo Collaboration Agreement, we received a one-time, non-refundable upfront payment of $195.0 million (see "Novo Collaboration Agreement"). In August 2025, we received a $12.5 million milestone payment from Vertex Pharmaceuticals Incorporated ("Vertex") (see "Vertex Asset Purchase Agreement").

We believe our cash, cash equivalents, and marketable securities of $548.7 million as of December 31, 2025 will be sufficient to fund our operations and capital expenditure requirements at least into 2029.

We use contract research and development organizations to conduct our preclinical works and clinical trials. Additionally, we utilize third-party contract manufacturing organizations ("CMOs"), to manufacture and supply our preclinical and clinical materials during the development of our product candidates. We expect to use similar contract resources for the commercialization of our products, at least until our resources and operations are at a scale that justifies investment in internal manufacturing capabilities.

We conduct research and manufacturing work outside of the U.S., including China, that may be affected by tariffs, including tariffs that have been or may in the future be imposed by the U.S. or other countries through reciprocal tariffs. While we do not currently believe tariffs will have a material impact on our business or results of operations, we will continue to carefully monitor the situation. Additionally, we continue to actively monitor macroeconomic conditions and market volatility resulting from global and national economic developments, political unrest, high inflation, disruptions in capital markets, changes in international trade relationships, changes in or the disruptions of U.S. governmental agencies, whether from a continued U.S. federal government shutdown or reduced resources, new laws and regulations or amendments to existing laws and regulations in the U.S. and foreign countries, and military conflicts. While we believe such factors have had no significant impact on our business or financial results during the periods presented, future developments and potential impacts on our business are uncertain and cannot be predicted with confidence.

Collaboration, Research Services, and Asset Purchase Agreements

Novo Collaboration Agreement

In May 2025, we entered into the Collaboration Agreement with Novo. Under the Novo Collaboration Agreement, we and Novo are exclusively collaborating to leverage our proprietary Native Complex Platform® to discover, develop and commercialize multiple potential oral small molecule therapies for metabolic-related diseases based on certain specified molecular targets. The collaboration objective is to discover and develop several novel mono-, dual-, or triple-acting oral small molecule drug candidates directed across five Collaboration Targets. The collaboration includes our most advanced preclinical metabolic program focused on developing an oral small molecule agonist to the GIP receptor. We and Novo have initially commenced four simultaneous research and development programs (each an "R&D Program") with each pursuing one or more Collaboration Targets from discovery through development candidate selection.

In July 2025, the Novo Collaboration Agreement became effective and, subsequently, we received a one-time, non-refundable upfront payment of $195.0 million, which was recorded as deferred revenue in our balance sheet. For each R&D Program, we are also eligible to receive up to approximately $498.0 million in research, development, regulatory, and commercial milestone payments. In addition, we are entitled to escalating, tiered royalties ranging from mid-to-high single-digits based on global product sales on a country-by-country and product-by-product basis with respect to a R&D Program until the later of ten years after the date of first commercial sale of the first product in such R&D Program in such country, expiration of specified patent rights covering such product in such country or the expiration of specified regulatory exclusivity for the first product in such R&D Program in such country. See Note 4 to the financial statements included elsewhere in this Annual Report for additional information.

Vertex Asset Purchase and Research Service Agreement

Vertex Asset Purchase Agreement

In September 2023, we entered into an asset purchase agreement with Vertex for a total of $47.6 million under which Vertex acquired all of our IPR&D asset related to a GPCR program, including all intellectual property, materials, and compounds associated with the program ("Vertex Asset Purchase Agreement"). Additionally, as part of the agreement, Vertex assumed all claims, counterclaims and credits associated with the program, and we gave up all rights to the intellectual property. The transfer of the IPR&D asset to Vertex was completed in November 2023.

The Vertex Asset Purchase Agreement also provided for a potential milestone payment payable to us contingent upon achievement of a certain research milestone. In July 2025, this milestone event was determined to have been achieved and, as a result, we received a payment of $12.5 million in August 2025, which was recorded as a gain on sale of the non-financial asset within total operating expenses in our statement of operations and comprehensive loss for the year ended December 31, 2025. Subsequently, there are no additional payments related to this IPR&D asset.

Vertex Research Service Agreement

In addition to the Vertex purchase agreement, we also entered into a research service agreement with Vertex ("Vertex Research Service Agreement") under which we agreed to perform certain exploratory research activities for Vertex. We recognized revenue associated with the Vertex Research Service Agreement over the performance period of the research services as the services were provided. The Vertex Research Service Agreement expired in September 2025.

Components of Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to do so in the foreseeable future. Our ability to generate product revenue, if ever, will depend on the successful development and eventual commercialization of any product candidates that we identify. If we fail to complete the development of any future product candidates in a timely manner or to obtain regulatory approval for such product candidates, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected. Our revenues to date have been exclusively related to license and research and development ("R&D") services. Our license and research service revenue consists of amounts recognized from the portions of the non-refundable upfront payment and R&D services performed by us.

Operating Expenses

Our operating expenses consist of (i) research and development expenses and (ii) general and administrative expenses.

Research and Development

Research and development expenses account for the largest component of our total operating expenses. Research and development expenses consist primarily of direct and unallocated costs incurred for the research and development of our product candidates.

Our research and development expenses consist of:

- Direct costs, including:
  - clinical program costs, which include external costs to conduct clinical trials, including costs paid to contract research organizations ("CROs"), the production of clinical materials and fees paid to contract manufacturers, costs incurred in connection with clinical laboratory operations, materials and supplies;
  - preclinical and research program costs, which include external research and development costs related to (i) the production of preclinical materials, including fees and milestones paid to contract manufacturers and (ii) agreements with contract development organizations, consultants and other third-party contract organizations to conduct our preclinical studies and other research and development activities on our behalf, costs incurred in connection with laboratory operations, materials and supplies, and other preclinical studies; and
- unallocated costs, including:
  - payroll-related costs, including salaries, benefits and stock-based compensation for employees engaged in research and development activities;

- external research and development costs, including contract research and development and professional service fees for consulting and related services;
- facility-related and office costs, including lease/rent, building-related expenses, facility-related overhead, and depreciation expense; and
- other costs, including expenses related to our funded, sponsored research activities and technology licenses, laboratory operations, information technology ("IT")-related expenses

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

A significant portion of our research and development costs have been external costs, which we track by stage of development. However, we do not track our unallocated costs on a program specific basis because these costs are deployed across multiple projects and, as such, are not separately classified.

At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We expect that our research and development expenses will increase substantially in absolute dollars for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, as our product candidates advance into later stages of development, as we begin to conduct new clinical trials, as we seek regulatory approvals for any product candidates that successfully complete clinical trials, and as we incur expenses associated with hiring additional personnel to support our research and development efforts. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with developing product candidates, many of which are outside of our control, including the uncertainty of:

- the scope, timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new ones;
- establishing an appropriate safety profile with IND-enabling studies;•the number of sites and patients included in the clinical trials;
- the number of sites and patients included in the clinical trials;
- the countries in which the clinical trials are conducted;
- our ability to replicate positive results from a completed clinical study in a future clinical study;
- per patient trial costs;
- successful patient enrollment in, and the initiation of, clinical trials, as well as drop out or discontinuation rates;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to FDA, EMA, or any other comparable foreign regulatory authorities;
- delays or disruptions in review, approval, inspection, or other actions by the FDA or other applicable U.S. or foreign government regulatory authorities that could impact the timing, initiation, conduct, or completion of our clinical trials or marketing applications;
- the number of trials required for regulatory approval;
- the timing, receipt and terms of any regulatory approvals from applicable regulatory authorities;
- our ability to maintain existing collaborations and strategic relationships, to identify and establish any future collaboration arrangements on favorable terms, if at all, and to realize the intended and potential benefits of such agreements and collaborations;
- the performance of any current or future collaborators;
- the performance of any current or future collaborators;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

- significant and changing government regulation and regulatory guidance;
- the impact of any business interruptions to our operations or to those of the third parties with whom we work;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- launching commercial sales of our product candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following regulatory approval.

Any changes in the outcome of any of these variables could mean a significant change in the costs and timing associated with the development of our product candidates. For example, if the FDA, EMA or any other comparable foreign regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development. We may never obtain regulatory approval for any of our product candidates.

General and Administrative

General and administrative expenses consist primarily of personnel-related costs, costs related to maintenance and filing of intellectual property, legal fees related to corporate matters, professional fees paid for accounting, auditing, consulting, tax and investor relations services, insurance costs, general corporate expenses, and IT-related and facility-related costs not otherwise included in research and development expenses. Personnel-related costs include salaries, benefits, and stock-based compensation for our personnel in executive, legal, finance and accounting, human resources, and other administrative functions.

We expect that our general and administrative expenses will increase substantially in absolute dollars for the foreseeable future as we continue to increase our headcount to support our business growth and to advance our research and development programs.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and marketable securities during the period.

Other Income (Expense), Net

Other income (expense), net consists primarily of changes in the fair value of our cash equivalents held in money market funds, loss on disposal of our fixed assets and foreign currency transaction gain or loss.

Benefit (Provision) for Income Taxes

We are subject to corporate U. S. federal and state income taxation. Our benefit for income taxes is recorded in accordance with Accounting Standard Codification 740, Accounting for Income Taxes, which provides for deferred taxes using an asset and liability approach. We establish a valuation allowance against all of our net deferred tax assets. We consider all available evidence, both positive and negative, including but not limited to our historical operating results, income or loss in recent periods, cumulative losses in recent years, forecasted earnings (losses), future taxable income (loss), and significant risk and uncertainty related to forecasts, and concluded the deferred tax assets are not more likely than not to be realized.

On July 4, 2025, the One Big Beautiful Bill Act ("H.R.1") was signed into law, which introduced significant changes to the U.S. federal income tax code. Among other changes, H.R.1 makes permanent key elements of the Tax Cuts and Jobs Act, including restoring 100% bonus depreciation, eliminating the capitalization requirement for domestic research and development expenses, and modifying the business interest expense limitation, which now allows depreciation and amortization to be included in the limitation calculation.

Results of Operations

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

	Years Ended December 31,		
	2025	2024	Change
Revenue	$ 45,951	$ 1,075	$ 44,876
Operating expenses:			
Research and development	97,584	65,337	32,247
General and administrative	29,164	16,561	12,603
Gain on sale of non-financial asset	(12,500)	—	(12,500)
Total operating expenses	114,248	81,898	32,350
Loss from operations	(68,297)	(80,823)	12,526
Other income, net:			
Interest income	19,530	8,617	10,913
Other (expense) income, net	(100)	(90)	(10)
Total other income, net	19,430	8,527	10,903
Loss before provision (benefit) for income taxes	(48,867)	(72,296)	23,429
Provision (benefit) for income taxes	12	(498)	(510)
Net loss	$ (48,879)	$ (71,798)	$ 22,919

Revenue

Our revenue was generated from research activities performed for Novo in connection with the Novo Collaboration Agreement and Vertex in connection with the Vertex Research Service Agreement.

$45.4 million of our total revenue for the year ended December 31, 2025 was generated from research activities performed for Novo in connection with the Novo Collaboration Agreement, of which $26.8 million was recognized from deferred revenue associated with our upfront payment, while the remainder was generated from research activities performed for Vertex in connection with the Vertex service agreement. All of our revenue for the year ended December 31, 2024 was generated from research activities performed for Vertex in connection with the Vertex service agreement.

Operating Expenses

Research and Development

The following table summarizes our research and development expenses for the periods indicated by direct and unallocated costs (in thousands):

	Years Ended December 31,		
	2025	2024	Change
Direct costs:			
PTH1R	$ 12,895	$ 11,719	$ 1,176
MRGPRX2	12,994	2,866	10,128
Other programs	26,526	4,222	22,304
Unallocated costs:			
Payroll-related expenses, including stock-based compensation	27,833	17,924	9,909
External research and development costs	3,486	15,287	(11,801)
Facility-related and office costs	8,365	6,390	1,975
Other costs	5,485	6,929	(1,444)
Total research and development expense	$ 97,584	$ 65,337	$ 32,247

Research and development expense was $97.6 million and $65.3 million for the years ended December 31, 2025 and 2024, respectively. The increase of $32.2 million was primarily due to (i) $22.3 million of higher direct costs attributable to increased spending with our other programs, (ii) $10.1 million of higher direct costs associated with our MRGPRX2 program, including an increase of $6.9 million in external clinical development expenses, (iii) $9.9 million of higher employee-related costs as a result of increased headcount as we grow our business, (iv) $2.0 million of higher facility-related and office costs as we expanded our office space to accommodate

higher occupancy and larger operational activities and (v) $1.2 million of increased direct costs associated with our PTH1R program. This was partially offset by a decrease of (i) $11.8 million in unallocated external research and development costs and (ii) $1.4 million in unallocated other costs. We expect to continue to incur increased research and development expenses as we advance SEP-631, SEP-479, and our other programs in our pipeline.

General and Administrative

General and administrative expenses were $29.2 million and $16.6 million for the years ended December 31, 2025 and 2024, respectively. The increase of $12.6 million was primarily due to (i) $6.1 million of higher employee-related costs as a result of increased headcount to support our growing operations, (ii) $2.5 million of higher legal fees, (iii) $2.0 million of higher IT operation expenses, and (iv) $2.0 million of higher facility costs, consulting and other expenses, primarily attributable to our operational growth and operating as a public company.

Gain on Sale of Non-Financial Asset

Gain on sale of non-financial asset of $12.5 million during the year ended December 31, 2025 was attributable to a milestone payment under the Vertex Asset Purchase Agreement. No gain on sale of non-financial asset was recorded during the year ended December 31, 2024.

Other Income, Net

Interest Income

Interest income was $19.5 million and $8.6 million for the years ended December 31, 2025 and 2024, respectively. The increase in interest income was due to higher average balances of invested cash in cash equivalents and marketable securities.

Provision (Benefit) for Income Taxes

Our income tax was not material for the year ended December 31, 2025. For the year ended December 31, 2024, we recorded a benefit for income taxes of $0.5 million.

Liquidity and Capital Resources

Sources of Liquidity

Our net loss was $48.9 million for the year ended December 31, 2025 compared to $71.8 million of net loss for the year ended December 31, 2024. As of December 31, 2025, we had an accumulated deficit of $167.3 million. We have incurred net losses in each year since inception, except for the year ended December 31, 2023. We expect to continue to incur net losses for the foreseeable future. Our net losses may fluctuate significantly from period to period, depending on the timing and expenditures of our operational activities.

We historically financed our operations primarily through the issuances of convertible promissory notes and convertible preferred stock, an IPO, and strategic collaborations with other companies. In October 2024, we completed our IPO, pursuant to which we issued and sold an aggregate of 18.4 million shares of common stock (inclusive of 2.4 million shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares). The aggregate net proceeds received by us from the IPO was $302.8 million, after deducting underwriting discounts and commissions, and other offering costs payable by us of $28.4 million. In July 2025, upon the effectiveness of the Novo Collaboration Agreement, we received a one-time, non-refundable upfront payment of $195.0 million. In August 2025, we received a $12.5 million milestone payment from the Vertex Asset Purchase Agreement.

As of December 31, 2025, we had $548.7 million in cash, cash equivalents, and marketable securities, which we believe will be sufficient to fund our operations and capital expenditure requirements at least into 2029.

We do not have any off-balance sheet arrangements other than our indemnification agreements as described in Note 7 to our audited financial statements included elsewhere in this Annual Report.

Cash Flows

The following table summarizes our cash flows for the periods indicated (in thousands):

	Years Ended December 31,	
	2025	2024
Net cash provided by (used in) operating activities	$ 110,189	$ (67,470)
Net cash used in investing activities	(229,352)	(160,598)
Net cash provided by financing activities	1,689	377,781
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (117,474)	$ 149,713

Net Cash Provided by (Used in) Operating Activities

Net cash provided by operating activities was $110.2 million for the years ended December 31, 2025. The net cash provided by operating activities for the year ended December 31, 2025 was due to $162.8 million of net change in operating assets and liabilities, primarily resulting from the upfront payment from the Novo Collaboration Agreement and $8.8 million of non-cash charges for depreciation and amortization, stock-based compensation, non-cash operating lease expense, accretion of premiums (discounts) on marketable securities, and other adjustments, which was partially offset by net loss of $48.9 million and gain on sale of non-financial asset of $12.5 million.

Net cash used in operating activities was $67.5 million for the years ended December 31, 2024. Net cash used in operating activities for the year ended December 31, 2024 was due to our net loss of $71.8 million, which was partially offset by (i) $4.1 million of non-cash charges for depreciation and amortization, stock-based compensation, non-cash operating lease expense, deferred income tax and accretion of premiums (discounts) on marketable securities and other adjustments, and (ii) $0.2 million of net change in operating assets and liabilities.

Net Cash Used in Investing Activities

Net cash used in investing activities of $229.4 million for the year ended December 31, 2025 was due to $451.0 million of purchases of marketable securities and $0.5 million of purchases of property and equipment, partially offset by the maturity of $209.6 million of marketable securities and the receipt of the $12.5 million milestone payment related to the Vertex Asset Purchase Agreement

Net cash provided by investing activities of $160.6 million for the year ended December 31, 2024 was due to $213.4 million of purchases of marketable securities and $2.1 million of purchases of property and equipment, partially offset by the receipt of the remaining $22.6 million from the sale of non-financial asset in 2023 and the maturity of $32.3 million of marketable securities.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $1.7 million for the year ended December 31, 2025 was primarily attributable to the proceeds from the exercise of stock options and employee stock purchase plan.

Net cash provided by financing activities was $377.8 million for the year ended December 31, 2024. Net cash provided by financing activities for the year ended December 31, 2024 was primarily due to $302.8 million of net proceeds from the issuance of our common stock in our IPO and $74.9 million of net proceeds from the sale and issuance of our Series B Convertible Preferred Stock.

Future Funding Requirements

Our primary use of cash, cash equivalents, and marketable securities is to fund our operations, primarily research and development expenditures. Cash, cash equivalents, and marketable securities used for operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable, accrued expenses and prepaid expenses.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, timing, progress and results of discovery, preclinical development, laboratory testing and clinical trials for our product candidates;

- our ability to successfully develop, obtain regulatory and marketing approvals of our product candidates for the expected indications and patient populations;
- the expenses of manufacturing our product candidates for clinical trials and in preparation for marketing approval and commercialization;
- our ability to maintain existing collaborations or strategic relationships and the extent to which we identify and enter into future collaborations or other arrangements with additional third parties in order to further develop our product candidates, as well as our ability to realize the intended and potential benefits of such agreements and collaborations;
- regulatory or legal developments in the United States and other countries;
- the expenses of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the expenses and fees associated with the discovery, acquisition or in-license of additional product candidates or technologies;
- our ability to establish additional collaborations on favorable terms, if at all;
- the expenses required to scale up our clinical, regulatory and manufacturing capabilities;
- the expenses of future commercialization activities, if any, including establishing sales, marketing, manufacturing and distribution capabilities, for any of our product candidates for which we receive marketing approval; and
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval.

We will need additional funds to meet operational needs and capital requirements for clinical trials, other research and development expenditures, and business development activities. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical studies.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. However, the trading prices for our common stock and for other biopharmaceutical companies have been highly volatile. As a result, we may face difficulties raising capital through sales of our common stock, and such sales may be on unfavorable terms. Similarly, adverse macroeconomic conditions and market volatility resulting from global and national economic developments, political unrest, high inflation, disruptions in capital markets, changes in international trade relationships, changes in or the disruptions of U.S. governmental agencies, whether from a continued U.S. federal government shutdown or reduced resources, global health crises, or other factors could materially and adversely affect our ability to consummate an equity or debt financing on favorable terms or at all. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, existing stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect existing stockholders' rights as common stockholders. Debt financing and 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 acquisitions or capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution 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 or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, 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.

We historically financed our operations primarily through the issuances of convertible promissory notes and convertible preferred stock, through an IPO, and strategic collaborations with other companies. In October 2024, we completed our IPO, which resulted in net proceeds of $302.8 million, net of total offering costs of $28.4 million. In July 2025, upon the effectiveness of the Novo Collaboration Agreement, we received a one-time, non-refundable upfront payment of $195.0 million. In August 2025, we received a $12.5 million milestone payment from the Vertex Asset Purchase Agreement. Since our inception, we have devoted substantially all of our resources to raising capital, organizing and staffing our company, business and scientific planning, conducting discovery and research and development activities, establishing, maintaining, and protecting our intellectual property portfolio, developing and progressing our product candidates and preparing for clinical trials, establishing arrangements with third parties for the manufacture of our product candidates and component materials, engaging in collaboration activities, and providing general and administrative support for these operations.

Critical Accounting Policies and Use of Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP"). The preparation of these 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 financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on 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 that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions and any such differences may be material. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

We account for revenue in accordance with ASC 606, "Revenue from Contracts with Customers" ("ASC 606"). Under ASC 606, we recognize revenue when the customer obtains control of the promised goods or services at an amount that reflects the consideration we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following four steps: (i) confirm we have a contract with a customer that creates enforceable rights and obligations; (ii) identify promised products or services to be transferred to a customer; (iii) determine the transaction price, or the amount it expects to receive, including an estimate of uncertain amounts subject to a constraint to ensure revenue is not recognized in an amount that would result in a significant reversal upon resolution of the uncertainty, is determinable and allocated to the performance obligations; and (iv) recognize revenue when or as performance obligations are satisfied.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct and are distinct in the context of the contract. To the extent a contract includes multiple promised goods and services, we apply judgment to determine whether promised goods and services are both capable of being distinct and are distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation. For arrangements that include multiple performance obligations, we allocate the transaction price to the identified performance obligations based on the standalone selling price of each distinct performance obligation. In instances where standalone selling price is not directly observable, we develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract using a cost plus margin approach, which is an estimation method used when standalone selling price is not directly observable. Key assumptions used within this estimation method may include full-time equivalent personnel effort and estimated external costs associated with the performance obligation.

The transaction price is determined based on the consideration to which we will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, we estimate the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in our judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation.

We satisfy performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided our performance, (ii) our performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) our performance does not create an asset with an alternative use to us and we have an enforceable right to payment for performance completed to date. If we do not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

Our revenues are primarily derived through our license and research and development service arrangements. Payments to us under these arrangements typically include one or more of the following: one-time, non-refundable upfront payment, research and development service funding, milestone and other contingent payments to us for the achievement of defined collaboration objectives and certain collaboration, research and development and commercial milestones, as well as royalties based on net sales of approved drugs.

Consideration received prior to revenue recognition is recorded as deferred revenue in the balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, non-current. Contract assets represent research and development services which have been

performed but have not yet been billed and are reduced when they are subsequently billed. Such contract assets include accounts receivable when our right to consideration is unconditional. For our current contracts, we recognize revenue as the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and, if over time, revenue recognized is based on the use of an input method.

When no remaining performance obligations are required of us, or following the completion of the performance obligation period, such amounts are recognized as revenue upon transfer of control of the goods or services to the customer.

The terms of our collaborative arrangements include one or more of the following

(i) *Licenses of intellectual property, or IP* - If the license to our IP is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from consideration allocated to the license when the license is transferred to the customer and the customer can use and benefit from the licenses. For a license that is determined not to be distinct, it is combined with other promises and we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluates the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. We generally recognize revenue using the cost incurred to date as compared to the total estimated cost of each performance obligation. The impact on revenue of changes in total estimated costs are recognized on a cumulative basis in the period that the change occurs. If estimates of the total cost change, or if contract amendments change the scope of the performance obligation, the required adjustments to revenue could be material.

(ii) *Customer options* - We evaluate the customer options for material rights or options to acquire additional goods or services at no incremental consideration or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until the option is exercised and performance obligations are satisfied. If an option is not exercised before the option right expires, we will accelerate and recognize all remaining revenue related to the material right performance obligation.

(iii) *Research and development services* - The promises under our collaboration agreement include research and development services to be performed by us for or on behalf of the customer. Payments or reimbursements resulting from our research and development efforts are recognized as the services are performed and presented on a gross basis because we are the principal for such efforts. Reimbursements are recognized in revenue in our statements of operations and comprehensive loss. Expenses incurred as part of our efforts to perform the research and development services are recognized in research and development expense in our statements of operations and comprehensive loss.

(iv) *Manufacturing services* - The promises under our collaboration agreement include manufacturing services to be performed by us. Payments or reimbursements resulting from our manufacturing services are recognized as the services are performed and presented on a gross basis because we are the principal for such efforts. Reimbursements are recognized in revenue in our statements of operations and comprehensive loss. Expenses incurred to perform the manufacturing services are recognized in research and development expense in our statements of operations and comprehensive loss.

(v) *Milestone payments* - At the inception of each arrangement that includes development or regulatory milestone payments, we evaluate the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's, such as regulatory approvals, are not considered probable of being achieved until those approvals are received, and therefore, consideration included in the transaction price is constrained. We applied the variable consideration allocation exception under ASC 606 whereby variable milestone payments are not estimated and included in the transaction price at inception. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

(vi) *Commercial milestone payments and royalties* - For arrangements that include sales-based royalties, including milestone payments based on levels of sales, if the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied)

Stock-Based Compensation

Stock-based compensation is measured based on the estimated grant date fair value of the award and is recognized as expense on a straight-line basis over the requisite service period (usually the vesting period). Forfeitures are accounted for in the period in which they occur.

In determining the fair value of the options granted and Employee Stock Purchase Plan ("ESPP") shares, we use the Black-Scholes option pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term — The expected term represents the period that our stock options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). We have very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants. We will continue to apply this process until a sufficient amount of historical information regarding employee exercise patterns and post-vesting employment termination behavior becomes available.

Expected Volatility — Due to our limited operating history and lack of company-specific historical volatility as a public company due to our recent IPO in October 2024, or implied volatility as a private company, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period, where available, equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, life cycle stage and area of specialty.

Risk-free Interest Rate — The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the options.

Expected Dividend — We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist primarily of employee-related costs, including salaries, benefits and stock-based compensation for employees engaged in research and development activities, costs related to research activities, preclinical studies and clinical trials, contract manufacturing for the production of clinical and preclinical materials, information technology-related costs, allocated overhead costs including facility-related expenses, consulting fees, costs related to laboratory operations and fees paid to other entities that conduct certain research and development activities on our behalf. Payments made prior to the receipt of goods and services to be used in research and development are deferred and recognized as expense in the period in which the related goods are received or services are rendered.

We have entered into agreements with outsourced contract manufacturing and development and clinical research vendors. We estimate accrued research and development expenses as of each balance sheet date based on facts and circumstances known at that time. We periodically confirm the accuracy of its estimates with internal management personnel and external service providers, and makes adjustments, if necessary. Research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development services provided, but not yet invoiced, are included in accrued expenses on the balance sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments made under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered.

Recent Accounting Pronouncements

See Note 2 to our audited financial statements included elsewhere in this Annual Report for more information.

Emerging Growth Company and Smaller Reporting Company Status

We qualify as "emerging growth company" under the Jumpstart Our Business Startups Act of 2012 ("JOBS Act"), which permits us to take advantage of an extended transition period to comply with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of accounting standards that have different effective dates for public and private companies until those standards would otherwise apply to private companies. We have elected to use this extended transition period under the JOBS Act until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to

companies that comply with new or revised accounting pronouncements as of public company effective dates. We could be an emerging growth company until the earliest to occur: (i) the last day of the fiscal year in which we have more than $1.235 billion in annual gross revenue; (ii) the date we qualify as a "large accelerated filers" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), with at least $700.0 million of equity securities held by non-affiliates; (iii) the issuance, in any three-year period, by us of more than $1.0 billion in non-convertible debt securities; or (iv) the last day of the fiscal year ending after the fifth anniversary of our IPO. Even after we no longer qualify as an emerging growth company, we may continue to qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million.

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

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

The information required by this item is presented at the end of this Annual Report beginning on page F-1. An index of those financial statements is found in Part IV, Item 15, Exhibits, Financial Statement Schedules, of this Annual Report.

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

None

Item 9A. Controls and Procedures.

Management's Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Our disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating the 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. As required by Rule 13a-15(b) or Rule 15d-15(b) promulgated by the SEC under the Exchange Act, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Annual Report. Based on the foregoing, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Annual Report at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles ("GAAP") and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that the Company's receipts and expenditures are being made only in accordance with authorizations of our management and board of directors; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, management assessed the effectiveness of our internal control over financial reporting as of December 31, 2025 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013 framework). Based on this evaluation, management has concluded that the Company maintained effective internal control over financial reporting as of December 31, 2025.

Changes in Internal Control Over Financial Reporting

There have been 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 fiscal quarter ended December 31, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

Our management, including our principal executive officer and principal financial officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, the effectiveness of any internal control over financial reporting is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Item 9B. Other Information.

Rule 10b5-1 Trading Plans

On October 20, 2025, Liz Bhatt, M.S., M.B.A., our President and Chief Operating Officer, adopted a pre-arranged trading plan for the sale, at the times and prices specified in the plan, of up to an aggregate of 41,000 shares of our common stock (comprised of shares issuable upon the exercise of option awards previously granted to Ms. Bhatt), which plan expires at the earlier of January 15, 2027, and the date upon which all authorized transactions thereunder are completed. Ms. Bhatt's trading plan is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act.

On October 31, 2025, Samira Shaikhly, our Chief People Officer, adopted a pre-arranged trading plan for the sale, at the times and prices specified in the plan, of up to an aggregate of 109,206 shares of our common stock (comprised of shares issuable upon the exercise of option awards previously granted to Ms. Shaikhly), which plan expires at the earlier of October 30, 2026, and the date upon which all authorized transactions thereunder are completed. Ms. Shaikhly's trading plan is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act.

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

The information required by this item will be included in our definitive proxy statement relating to our 2026 Annual Meeting of Stockholders (the "Proxy Statement"), which we will file with the Securities and Exchange Commission (the "SEC") not later than 120 days after the end of our fiscal year ended December 31, 2025 and is incorporated in this Annual Report on Form 10-K (this "Annual Report") by reference.

We have adopted a code of business conduct and ethics (the "Ethics Code"), that applies to all our employees, officers and directors. This includes our principal executive officer, principal financial officer and principal accounting officer, or persons performing similar functions. The full text of the Ethics Code is available on our website at *www.septerna.com*. If we ever were to amend or waive any provision of our Ethics Code that applies to the Company's principal executive officer, principal financial officer, principal accounting officer, or any person performing similar functions, we intend to satisfy our disclosure obligations, if any, with respect to any such waiver or amendment by posting such information on our website set forth above rather than by filing a Current Report on Form 8-K. Information contained in, or that can be accessed through, our website is not incorporated by reference herein, and you should not consider information on our website to be part of this Annual Report.

Item 11. Executive Compensation

The information required by this item (excluding information under the subheading "Pay Versus Performance") will be included in the Proxy Statement and is incorporated in this Annual Report by reference.

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

The information required by this item will be included in the Proxy Statement and is incorporated in this Annual Report by reference.

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

The information required by this item will be included in the Proxy Statement and is incorporated in this Annual Report by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be included in the Proxy Statement and is incorporated in this Annual Report by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) *Financial Statements.* The financial statements of Septerna, Inc. and the report of Ernst & Young LLP, Independent Registered Public Accounting Firm, are included in a separate section of this Annual Report on Form 10-K beginning on page F-1. All financial statement schedules are omitted because the information is inapplicable or the information required is presented in our financial statements and notes thereto.

(b) *Exhibits*. The following is a list of exhibits filed as part of this Annual Report on Form 10-K:

		Incorporated by Reference			
Exhibit Number	**Description**	**Form**	**File No.**	**Exhibit**	**Filing Date**
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-42382	3.1	October 28, 2024
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-42382	3.2	October 28, 2024
4.1†	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated as of June 28, 2023	S-1	333-282469	4.1	October 24, 2024
4.2	Specimen Common Stock Certificate	S-1	333-282469	4.2	October 24, 2024
4.3*	Description of Securities of the Registrant				
10.1#	2021 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder	S-1	333-282469	10.1	October 21, 2024
10.2#	2024 Stock Option and Incentive Plan and forms of award agreements thereunder	S-1	333-282469	10.2	October 21, 2024
10.3#	2024 Employee Stock Purchase Plan	S-1	333-282469	10.3	October 21, 2024
10.4#	Form of Non-Employee Director Indemnification Agreement, by and between the Registrant and each of its non-employee directors	S-1	333-282469	10.4	October 21, 2024
10.5#	Form of Employee Director / Officer Indemnification Agreement, by and between the Registrant and each of its executive officers	S-1	333-282469	10.5	October 21, 2024
10.6#†	Employment Agreement, by and between the Registrant and Jeffrey Finer, dated as of September 9, 2022	S-1	333-282469	10.6	October 21, 2024
10.7#†	Employment Agreement, by and between the Registrant and Ran Xiao, dated as of January 18, 2022	S-1	333-282469	10.7	October 21, 2024
10.8#†	Employment Agreement, by and between the Registrant and Liz Bhatt, dated as of May 20, 2022	S-1	333-282469	10.8	October 21, 2024
10.9#†	Employment Agreement, by and between the Registrant and Jae B. Kim, dated as of September 4, 2024	S-1	333-282469	10.9	October 21, 2024
10.10#†	Employment Agreement, by and between the Registrant and Samira Shaikhly, dated as of December 22, 2022	S-1	333-282469	10.10	October 21, 2024
10.11#†	Employment Agreement, by and between the Registrant and Uwe Klein, dated as of February 17, 2021	S-1	333-282469	10.11	October 21, 2024
10.12#†	Employment Agreement, by and between the Registrant and Daniel Long, dated as of September 27, 2021	S-1	333-282469	10.12	October 21, 2024
10.13#	Amended and Restated Non-Employee Director Compensation Policy	10-Q	001-42382	10.1	November 10, 2025
10.14#	Senior Executive Cash Incentive Bonus Plan	S-1	333-282469	10.14	October 21, 2024
10.15#	Offer Letter, by and between the Company and Gil M. Labrucherie, dated as of December 6, 2024.	8-K	001-42382	10.1	January 6, 2025
10.16#	Executive Severance Plan of the Registrant	S-1	333-282469	10.16	October 21, 2024

10.17†	Lease Agreement, by and between the Registrant and Britannia Pointe Grant Limited Partnership, dated as of April 20, 2021, as amended by the First Amendment to Lease Agreement dated as of September 14, 2022, Second Amendment to Lease Agreement dated as of September 23, 2022, Third Amendment to Lease Agreement dated as of December 22, 2022, and Fourth Amendment to Lease Agreement dated as of December 12, 2023	S-1	333-282469	10.17	October 21, 2024
10.18	Service Agreement, by and between the Registrant and Third Rock Ventures, LLC, dated as of August 25, 2021	S-1	333-282469	10.18	October 21, 2024
10.19**	Novo Collaboration Agreement, between the Registrant and Novo Nordisk A/S, dated as of May 13, 2025	10-Q	001-42382	10.1	August 11, 2025
10.20*#	Employment Agreement, by and between the Registrant and Mark Wilson, dated as of January 6, 2026				
19.1	Insider Trading Policy of the Registrant	10-K	001-42382	19.1	March 27, 2025
21.1	Subsidiaries of the Registrant	S-1	333-282469	21.1	October 21, 2024
23.1*	Consent of Independent Registered Public Accounting Firm				
24.1*	Power of Attorney (included on signature page)				
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1*+	Certifications of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
97.1#	Compensation Recovery Policy of the Registrant	S-1	333-282469	10.15	October 21, 2024
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				
101.SCH*	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents				
104*	Cover Page formatted as Inline XBRL and contained in Exhibit 101				

* Filed herewith.

** Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the SEC because the Registrant has determined that information is both not material and is the type that the registrant treats as private or confidential.

+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Annual Report and will not be deemed to be "filed" for purposes of Section 18 of the Exchange Act, except to the extent that the Registrant specifically incorporates it by reference.

# Indicates a management contract or any compensatory plan, contract or arrangement.
† Annexes, schedules and/or exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of any omitted attachment to the SEC on a confidential basis upon request.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

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

Septerna, Inc.

Date: March 9, 2026

By: /s/ Jeffrey Finer, M.D., Ph.D.
Jeffrey Finer, M.D., Ph.D.
Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

KNOW ALL BY THESE PRESENT, that each individual whose signature appears below hereby constitutes and appoints each of Jeffrey Finer and Gil M. Labrucherie, as such person's true and lawful attorney-in-fact and agent with full power of substitution and resubstitution, for such person in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent 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 such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following person in the capacities and on the date indicated.

Name	Title	Date
/s/ Jeffrey Finer, M.D., Ph.D. Jeffrey Finer, M.D., Ph.D.	Chief Executive Officer and Director (principal executive officer)	March 9, 2026
/s/ Gil M. Labrucherie, CFA, J.D. Gil M. Labrucherie, CFA, J.D.	Chief Financial Officer (principal financial officer and principal accounting officer)	March 9, 2026
/s/ Jeffrey Tong, Ph.D. Jeffrey Tong, Ph.D.	Chairman and Director	March 9, 2026
/s/ Abraham Bassan, M.S. Abraham Bassan, M.S.	Director	March 9, 2026
/s/ Bernard Coulie, M.D., Ph.D., M.B.A. Bernard Coulie, M.D., Ph.D., M.B.A.	Director	March 9, 2026
/s/ Alan Ezekowitz, M.D., D.Phil. Alan Ezekowitz, M.D., D.Phil.	Director	March 9, 2026
/s/ Shalini Sharp, M.B.A. Shalini Sharp, M.B.A.	Director	March 9, 2026
/s/ Jake Simson, Ph.D. Jake Simson, Ph.D.	Director	March 9, 2026
/s/ Keith Gottesdiener, M.D. Keith Gottesdiener, M.D.	Director	March 9, 2026

SEPTERNA, INC.

INDEX TO FINANCIAL STATEMENTS

Financial Statements as of and for the Years Ended December 2025 and 2024

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of
Septerna, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Septerna, Inc. (the Company) as of December 31, 2025 and 2024, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity, 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 "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at 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.

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 2023.

San Mateo, California
March 9, 2026

SEPTERNA, INC.

Balance Sheets
(In thousands, except for share and per share data)

	As of December 31,	
	2025	2024
Assets		
Current assets:		
Cash and cash equivalents	$ 120,722	$ 238,196
Marketable securities	270,367	112,727
Accounts receivable	10,356	171
Prepaid expenses and other current assets	9,519	5,730
Total current assets	410,964	356,824
Marketable securities, non-current	157,569	69,866
Property and equipment, net	4,434	5,090
Operating lease right-of-use assets	21,499	23,602
Restricted cash	905	905
Other non-current assets	816	267
Total assets	$ 596,187	$ 456,554
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 10,283	$ 3,200
Accrued expenses and other current liabilities	12,167	7,798
Deferred revenue, current	62,269	—
Operating lease liabilities, current	2,212	1,851
Total current liabilities	86,931	12,849
Deferred revenue, non-current	105,917	—
Operating lease liabilities, non-current	21,413	23,625
Other non-current liabilities	—	33
Total liabilities	214,261	36,507
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized as of December 31, 2025 and December 31, 2024; no shares issued and outstanding as of December 31, 2025 and December 31, 2024	—	—
Common stock, $0.001 par value per share, 500,000,000 shares authorized at December 31, 2025 and December 31, 2024; 44,806,272 and 44,422,505 shares issued and outstanding at December 31, 2025 and December 31, 2024 respectively; 131,224 and 576,829 shares subject to repurchase as of December 31, 2025 and December 31, 2024, respectively	45	44
Additional paid-in capital	548,517	538,321
Accumulated other comprehensive income	617	56
Accumulated deficit	(167,253)	(118,374)
Total stockholders' equity	381,926	420,047
Total liabilities and stockholders' equity	$ 596,187	$ 456,554

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

SEPTERNA, INC.

Statements of Operations and Comprehensive Loss
(In thousands, except for share and per share data)

	Years Ended December 31,	
	2025	2024
Revenue	$ 45,951	$ 1,075
Operating expenses:		
Research and development	97,584	65,337
General and administrative	29,164	16,561
Gain on sale of non-financial asset	(12,500)	—
Total operating expenses	114,248	81,898
Loss from operations	(68,297)	(80,823)
Other income, net:		
Interest income	19,530	8,617
Other expense, net	(100)	(90)
Total other income, net	19,430	8,527
Loss before provision (benefit) for income taxes	(48,867)	(72,296)
Provision (benefit) for income taxes	12	(498)
Net loss	$ (48,879)	$ (71,798)
Net loss per share, basic and diluted	(1.10)	(7.26)
Weighted-average shares outstanding, basic and diluted	44,258,338	9,891,126
Comprehensive loss:		
Net loss	$ (48,879)	$ (71,798)
Net unrealized gain on marketable securities	561	56
Total other comprehensive income	561	56
Comprehensive loss	$ (48,318)	$ (71,742)

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

SEPTERNA, INC.

Statements of Convertible Preferred Stock and Stockholders' Equity

(In thousands, except for share data)

	Convertible Preferred Stock									
	Series A		Series B		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2023	75,000,000	$ 74,694	60,828,720	$ 74,521	3,168,134	$ 3	$ 8,199	$ —	$ (46,576)	$ (38,374)
Issuance of Series B Convertible Preferred Stock, net of issuance costs of $58	—	—	60,828,732	74,942	—	—	—	—	—	—
Issuance of common stock in connection with initial public offering, net of issuance costs of $28,431	—	—	—	—	18,400,000	18	302,749	—	—	302,767
Conversion of convertible preferred stock to common stock upon initial public offering	(75,000,000)	(74,694)	(121,657,452)	(149,463)	22,839,774	23	224,134	—	—	224,157
Issuance of common stock upon exercise of stock options	—	—	—	—	28,896	—	66	—	—	66
Vesting of restricted common stock	—	—	—	—	—	—	21	—	—	21
Repurchases of unvested restricted common stock	—	—	—	—	(14,299)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	3,152	—	—	3,152
Net unrealized gain on marketable securities	—	—	—	—	—	—	—	56	—	56
Net loss	—	—	—	—	—	—	—	—	(71,798)	(71,798)
Balance at December 31, 2024	—	—	—	—	44,422,505	44	538,321	56	(118,374)	420,047
Issuance of common stock upon exercise of stock options	—	—	—	—	268,188	1	981	—	—	982
Issuance of common stock under employee stock purchase plan	—	—	—	—	118,191	—	717	—	—	717
Vesting of restricted common stock	—	—	—	—	—	—	23	—	—	23
Repurchases of unvested restricted common stock	—	—	—	—	(2,612)	—	(1)	—	—	(1)
Stock-based compensation expense	—	—	—	—	—	—	8,476	—	—	8,476
Net unrealized gain on marketable securities	—	—	—	—	—	—	—	561	—	561
Net loss	—	—	—	—	—	—	—	—	(48,879)	(48,879)
Balance at December 31, 2025	—	$ —	—	$ —	44,806,272	$ 45	$ 548,517	$ 617	$ (167,253)	$ 381,926

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

SEPTERNA, INC.

Statements of Cash Flows
(In thousands)

	Years Ended December 31,	
	2025	2024
Cash flows from operating activities:		
Net loss	$ (48,879)	$ (71,798)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation and amortization	1,604	1,401
Gain on sale of non-financial asset	(12,500)	—
Non-cash operating lease expense	2,103	1,383
Stock-based compensation	8,476	3,152
Accretion of discounts, net	(3,448)	(1,410)
Deferred income tax	—	(491)
Other	56	45
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(3,781)	(4,297)
Accounts receivable	(10,185)	(20)
Other non-current assets	(554)	(170)
Accounts payable	6,603	723
Accrued expenses and other current liabilities	4,359	3,564
Deferred revenue	168,186	—
Operating leases, net	(1,851)	448
Net cash provided by (used in) operating activities	110,189	(67,470)
Cash flows from investing activities:		
Purchases of property and equipment	(518)	(2,103)
Proceeds from sale of non-financial asset	12,500	22,625
Purchases of available-for-sale marketable securities	(450,950)	(213,390)
Maturities of available-for-sale marketable securities	209,616	32,270
Net cash used in investing activities	(229,352)	(160,598)
Cash flows from financing activities:		
Proceeds from Initial Public Offering, net of offering costs	—	302,788
Proceeds from issuance of Series B Convertible Preferred Stock, net of issuance costs	—	74,942
Repurchases of unvested restricted common stock	(1)	(1)
Proceeds from exercise of stock options	973	52
Proceeds from employee stock purchase plan	717	—
Net cash provided by financing activities	1,689	377,781
Net (decrease) increase in cash, cash equivalents and restricted cash	(117,474)	149,713
Cash, cash equivalents and restricted cash, beginning of year	239,101	89,388
Cash, cash equivalents and restricted cash, end of year	$ 121,627	$ 239,101
Supplemental cash flow information:		
Cash paid for income taxes	$ —	$ 232
Supplemental disclosure for noncash investing and financing activities:		
Property and equipment included in accounts payable and accrued expenses and other current liabilities	$ 517	$ 37
Right-of-use asset recognized in exchange for operating lease liability	$ —	$ 12,462
Conversion of convertible preferred stock to common stock upon initial public offering	$ —	$ 224,157
Unpaid offering costs included in accounts payable	$ —	$ 21

Cash, Cash Equivalents and Restricted Cash:

	As of December 31,	
	2025	2024
Cash and cash equivalents	$ 120,722	$ 238,196
Restricted cash	905	905
Total cash, cash equivalents and restricted cash at end of year	$ 121,627	$ 239,101

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

1. Organization

Description of the Business

Septerna, Inc. ("Septerna" or the "Company") is a clinical-stage biotechnology company with a world-class team of G protein-coupled receptor ("GPCR") experts and drug developers advancing cutting-edge science to unlock the full potential of GPCR therapies for patients with significant unmet needs. The Company's proprietary Native Complex Platform® is designed to enable new approaches to GPCR drug discovery and has led to the development of a diverse pipeline of novel oral small molecule drug candidates. The Company is advancing programs in endocrinology, immunology and inflammation, metabolic diseases and additional therapeutic areas, both independently and with partners.

The Company's proprietary Native Complex Platform® replicates the natural structure, function, and dynamics of GPCRs outside of cells at an industrial scale. The Company's foundational technologies enable it to isolate, purify, and reconstitute full-length, properly folded GPCR proteins within ternary complexes with ligands and transducer proteins in a lipid bilayer that mimics the cell membrane. The Company then applies state-of-the-art discovery tools and technologies to these defined and tunable protein complexes to structurally design, screen for, and optimize potential product candidates. Leveraging its platform, the Company has transformed GPCR oral small molecule drug discovery to an industrialized and iterative structure-based drug design approach to expand the landscape of druggable GPCR targets with novel oral small molecule medicines for patients. The Company's Native Complex Platform® is designed to enable it to target certain GPCRs for the first time, uncover novel binding pockets for validated receptors, and pursue a wide spectrum of pharmacologies, including agonists, antagonists, and allosteric modulators, to affect GPCR signaling in different ways to achieve desired therapeutic effects.

The Company was incorporated in Delaware in December 2019, under the name GPCR NewCo, Inc. In June 2021, the Company changed its name to Septerna, Inc. The Company is headquartered in South San Francisco, California.

Reverse Stock Split

On October 18, 2024, the Company effected a 1-for-8.6103 reverse stock split of its issued and outstanding shares of common stock. Upon the effectiveness of the reverse stock split, (i) all shares of outstanding common stock were adjusted; (ii) the conversion ratio of the convertible preferred stock was adjusted; (iii) the number of shares of common stock for which each outstanding option to purchase common stock is exercisable were adjusted; and (iv) the exercise price of each outstanding option to purchase common stock was adjusted. All of the outstanding common stock (including shares of common stock subject to the Company's options and as converted for the outstanding convertible preferred stock), share prices, exercise prices and per share amounts contained in the financial statements have been retroactively adjusted to reflect this reverse stock split for all periods presented. The par value per share and the authorized number of shares of common stock and preferred stock were not adjusted as a result of the reverse stock split. The number of authorized shares did not change.

Initial Public Offering

In October 2024, the Company completed its initial public offering ("IPO"), pursuant to which it issued and sold an aggregate of 18.4 million shares of its common stock at the IPO price of $18.00 per share, including 2.4 million shares that were issued to the underwriters pursuant to the full exercise of their option to purchase additional shares, resulting in net proceeds of $302.8 million, after deducting underwriting discounts and commissions of $23.2 million, and other offering expenses payable by the Company of $5.2 million. Immediately prior to the closing of the IPO, the Company's then outstanding convertible preferred stock automatically converted into 22,839,774 shares of common stock.

Following the closing of the IPO, no shares of convertible preferred stock were authorized or outstanding. In connection with the completion of the IPO, on October 28, 2024, the Company's certificate of incorporation was amended and restated to (i) authorize 500.0 million shares of common stock, par value $0.001 per share, which eliminates all references to the previously existing series of convertible preferred stock; and (ii) authorize 10.0 million shares of undesignated preferred stock, par value $0.001 per share, that may be issued from time to time by the Company's board of directors in one or more series.

Liquidity and Capital Resources

The accompanying financial statements have been prepared assuming the Company will continue as a going concern, which assumes that the Company will realize its assets and satisfies its liabilities in the normal course of business. The Company is subject to risks inherent in operating an early-stage biotechnology business. These risks include, but are not limited to, dependence on the development of marketable products, the ability to attract, retain, and motivate qualified personnel, rapid technological changes and the rapidly evolving nature of the biotechnology industry.

The Company has incurred significant losses and cumulative negative cash flows from operations since its inception and expects to incur losses as a result of its continued research and development activities. To date, none of the Company's product candidates have been approved by the U.S. Food and Drug Administration (the "FDA") for commercial sale and, therefore, the Company has not generated any revenue from product sales.

For the year ended December 31, 2025, the Company incurred net loss of $48.9 million. The Company had an accumulated deficit of $167.3 million as of December 31, 2025. The Company believes its cash, cash equivalents, and marketable securities of $548.7 million as of December 31, 2025 will be sufficient to fund its operations for, at least, 12 months from the date of issuance of the financial statements.

The Company historically financed its operations primarily through the issuance of convertible promissory notes, convertible preferred stock, the sale of its common stock in an IPO, and most recently, through a one-time, non-refundable upfront payment upon commencement of its collaboration agreement with Novo Nordisk A/S ("Novo") and achievement of a milestone event pursuant to its agreement with Vertex Pharmaceuticals Incorporated ("Vertex"). The Company expects to continue to generate operating losses for the foreseeable future. The Company will need additional financing to support its continuing operations and pursue its growth strategy. It expects to finance its operations through equity offerings, debt financings or other capital sources, including collaborations with other companies or other strategic transactions. The Company may not be able to obtain funding on acceptable terms, or at all. Any failure to raise capital as and when needed would compromise the Company's ability to execute on its business plan and may cause the Company to significantly delay, scale back or discontinue the research and development of some of its programs or curtail any efforts to expand its product pipelines and will materially harm its business, financial position and results of operations.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"), stated in U.S. dollars and include all adjustments necessary for the fair presentation of the Company's financial statements as of December 31, 2025 and 2024, and for the years then ended. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification and Accounting Standards Updates ("ASUs"), of the Financial Accounting Standards Board ("FASB").

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 and disclosures at the date of the financial statements and reported amounts of expenses during the reporting periods. These estimates form the basis for judgments the Company makes about the carrying values of assets and liabilities that are not readily apparent from other sources. The Company bases its estimates using historical experience, Company forecasts and future plans, current economic conditions, and information from third-party professionals that management believes to be 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 and adjusts those estimates and assumptions when facts and circumstances dictate. Estimates are used in determining the fair value of assets and liabilities, the useful lives of property and equipment, the rate used in determining the present value of lease payments, fair value of assets and liabilities, research and development accruals, the estimated fair value of common stock prior to the Company's IPO and assumptions used in stock-based compensation, the initial allocation and continued evaluation of a revenue contract's transaction price to each distinct performance obligation on a relative standalone selling price basis, uncertain tax positions and the valuation allowance for deferred income tax assets. Actual results may differ from these estimates and assumptions. As appropriate, we assess estimates each period, update them to reflect current information, and will generally reflect any changes in estimates in the period first identified.

The Company's results can also be affected by economic, political, legislative, regulatory and legal actions. Economic conditions, such as recessionary trends, inflation, interest, tariffs, changes in regulatory laws and monetary exchange rates, and government fiscal policies, can have a significant effect on operations. While the Company maintains reserves for anticipated liabilities, the Company could be affected by civil, criminal, regulatory or administrative actions, claims or proceedings.

Segment Information

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the chief operating decision maker ("CODM"), in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its chief executive officer. Based on the information used by the CODM to allocate resources, the Company has determined it operates in one segment.

Risks and Uncertainties

Financial instruments, which potentially subject the Company to a concentration of credit risk, consist primarily of cash, cash equivalents, marketable securities, and accounts receivable. The Company limits its credit risk by placing its cash, cash equivalents, and marketable securities with banks and institutions that are highly creditworthy. Such cash may be in excess of the Federal Deposit Insurance Corporation ("FDIC") insured limits, and the Company's cash equivalents and marketable securities are not insured by the FDIC. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash, cash equivalents and marketable securities to the extent recorded in the balance sheet.

The primary focus of the Company's investment strategy is to preserve capital and meet liquidity requirements. Management believes that the Company is not exposed to significant credit risk due to the high-credit-quality financial institutions in which those deposits are held. The Company has not experienced any losses on its cash, cash equivalents and marketable securities since inception. The Company has no significant off-balance sheet concentrations of credit risk.

The Company is subject to all of the risks inherent in an early-stage biotechnology company. These risks include, but are not limited to, efficacy of product candidates, intense competition, and dependence upon the availability of liquidity to sustain operations.

Cash Equivalents and Marketable Securities

The Company holds marketable securities that consist of highly liquid, investment grade debt securities. The Company's cash and marketable securities are held or issued by financial institutions that management believes are of high credit quality. Marketable securities are classified and accounted for as available-for-sale. Marketable securities with original maturities of 90 days or less are classified as cash equivalents. Marketable securities with original maturities over 90 days and remaining maturities of less than 12 months are classified as current. Marketable securities with remaining maturities of more than 12 months for which the Company has the intent and ability to hold the security for more than 12 months are classified as non-current. The Company's marketable securities are carried at estimated fair value, which is derived from independent pricing sources based on quoted prices in active markets for similar securities. Unrealized gains and losses are reported in stockholders' equity as accumulated other comprehensive income. The amortized cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income on the statements of operations and comprehensive loss.

The Company has the ability, if necessary, to liquidate any of its cash equivalents and marketable securities to meet its liquidity needs in the next 12 months. The Company does not generally intend to sell the investments and it is less likely that it will be required to sell the investments before recovery of their amortized cost bases, which may be at maturity.

The Company reviews its portfolio of marketable securities, using both quantitative and qualitative factors, to determine if declines in fair value below amortized cost have resulted from a credit-related loss or other factors. If the decline in fair value is due to credit-related factors, the Company recognizes a loss in its statement of operations and comprehensive loss, whereas if the decline in fair value is not due to credit-related factors, the Company records the loss in accumulated other comprehensive income on its balance sheets.

The Company excludes the applicable accrued interest from both the fair value and amortized cost basis of marketable securities for purposes of identifying and measuring an impairment. Accrued interest receivable on marketable securities is recorded within prepaid expenses and other current assets on the balance sheets. The Company's accounting policy is to not measure an allowance for credit loss for accrued interest receivable and to write-off any uncollectible accrued interest receivable as a reversal of interest income in a timely manner, which is considered to be in the period in which it is determined the accrued interest will not be collected.

Restricted Cash

Restricted cash is comprised of cash that is restricted as to withdrawal or use under the terms of certain contractual agreements. In connection with the Company's lease agreement (see Note 6), the Company is required to maintain a collateral account to secure a letter of credit issued to its landlord. The collateral account is classified as restricted cash on the Company's balance sheets. As of

December 31, 2025 and 2024, the remaining term of the leases is greater than one year and the related restricted cash is classified as non-current on the Company's balance sheet.

Deferred Revenue

Deferred revenue consists of amounts received prior to satisfying revenue recognition criteria (see Note 4).

Accounts Receivable

The Company recognizes a receivable when the Company has an unconditional right to payment, which is generally at the time of delivery of assets, or at the time services are rendered.

An allowance for expected credit losses over the life of the receivables is reserved for based on a combination of historical experience, aging analysis, current economic trends and information on specific accounts, with related amounts recorded as a reserve against revenue recognized. The reserve is re-evaluated on a regular basis and adjusted as needed. Once a receivable is deemed to be uncollectible, such balance is charged against the reserve. No allowance for credit losses was recorded during the years ended December 31, 2025 and 2024.

As of December 31, 2025, the Company’s accounts receivable was entirely attributable to Novo. As of December 31, 2024, the Company’s accounts receivable was entirely attributed to Vertex.

Property and Equipment, Net

Property and equipment is recorded at cost, subject to adjustments for impairments, less accumulated depreciation and amortization. The Company depreciates property and equipment using the straight-line method over the estimated useful lives of the respective assets, as follows:

Lab equipment	5 years
Furniture and fixtures	5 years
Office equipment	5 years
Computer Equipment	3 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Depreciation or amortization begins at the time the asset is placed in service. Maintenance and repairs that do not improve or extend the life of the respective asset are charged to expense as incurred. Upon disposal of assets, the cost and related accumulated depreciation or amortization is removed from the balance sheet and the resulting gain or loss is recognized within other income, net in the statements of operations and comprehensive loss.

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparing the carrying amount of each asset to the undiscounted expected future cash flows the asset is expected to generate over its remaining life. An impairment loss would be recognized when the estimated undiscounted future cash flows expected to result from the use of the asset or asset group and its eventual disposition are less than its carrying amount. Impairment, if any, is measured as the amount by which the carrying amount of a long-lived asset or asset group exceeds its fair value. There were no impairments of the Company’s long-lived assets for the years ended December 31, 2025 and 2024.

Leases

The Company accounts for its leases in accordance with FASB Accounting Standards Codification (“ASC”) 842, *Leases* (“ASC 842”). The Company adopted ASC 842 on January 1, 2021, prior to entering into the lease agreement for its office and research and development space. At inception of a contract, the Company determines whether an arrangement is or contains a lease. For each lease, the Company determines the classification as either an operating lease or a financing lease. Lease recognition occurs at the lease commencement date and lease liability amounts are determined based on the present value of lease payments over the lease term. The lease term may include options to extend or terminate the lease only when it is reasonably certain that the Company will exercise that option.

The Company uses its incremental borrowing rate based on the information available at lease commencement date in determining the present value of lease payments if the Company's leases do not provide an implicit rate. The Company determines its incremental borrowing rate based on the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment. Right-of-use assets represent the Company's right to use underlying assets for the lease term and operating lease liabilities represent the Company's obligation to make lease payments under the lease. Right-of-use assets also include any lease payments made prior to the commencement date and exclude lease incentives received.

The Company elected to apply the practical expedient of combining lease and non-lease components for the real estate lease asset class. Fixed lease payments on operating leases are recognized as lease expense over the expected term of the lease on a straight-line basis. Variable lease expenses that are not considered fixed are recognized as incurred.

In addition, the Company elected the short-term lease practical expedient that allows the lessee to not record a lease liability and right-of-use asset for all leases with a term of 12 months or less. See Note 6 for additional information on the Company's leases.

Revenue Recognition

The Company accounts for revenue in accordance with ASC 606, "Revenue from Contracts with Customers" ("ASC 606"). Under ASC 606, the Company recognizes revenue when the customer obtains control of the promised goods or services at an amount that reflects the consideration the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following four steps: (i) confirm it has a contract with a customer that creates enforceable rights and obligations; (ii) identify promised products or services to be transferred to a customer; (iii) determine the transaction price, or the amount it expects to receive, including an estimate of uncertain amounts subject to a constraint to ensure revenue is not recognized in an amount that would result in a significant reversal upon resolution of the uncertainty, is determinable and allocated to the performance obligations; and (iv) recognize revenue when or as performance obligations are satisfied.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct and are distinct in the context of the contract. To the extent a contract includes multiple promised goods and services, the Company applies judgment to determine whether promised goods and services are both capable of being distinct and are distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation. For arrangements that include multiple performance obligations, the Company allocates the transaction price to the identified performance obligations based on the standalone selling price of each distinct performance obligation. In instances where standalone selling price is not directly observable, the Company develops assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract using a cost plus margin approach, which is an estimation method used when standalone selling price is not directly observable. Key assumptions used within this estimation method may include full-time equivalent personnel effort and estimated external costs associated with the performance obligation.

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in management's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation.

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the Company's performance, (ii) the Company's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the Company's performance does not create an asset with an alternative use to the Company and the Company has an enforceable right to payment for performance completed to date. If the Company does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

The Company's revenues are primarily derived through its license and research and development service arrangements. Payments to the Company under these arrangements typically include one or more of the following: one-time, non-refundable upfront payment, research and development service funding, milestone and other contingent payments to the Company for the achievement of defined collaboration objectives and certain collaboration, research and development and commercial milestones, as well as royalties based on net sales of approved drugs.

Consideration received prior to revenue recognition is recorded as deferred revenue in the balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, non-current. Contract assets represent research and development services which have been performed but have not yet been billed and are reduced when they are subsequently billed. Such contract assets include accounts receivable when the Company's right to consideration is unconditional. For its current contracts, the Company recognizes revenue as the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and, if over time, revenue recognized is based on the use of an input method.

When no remaining performance obligations are required of the Company, or following the completion of the performance obligation period, such amounts are recognized as revenue upon transfer of control of the goods or services to the customer.

The terms of the Company's collaborative arrangements include one or more of the following

(i) *Licenses of intellectual property, or IP* - If the license to the Company's IP is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from consideration allocated to the license when the license is transferred to the customer and the customer can use and benefit from the licenses. For a license that is determined not to be distinct, it is combined with other promises and the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The Company generally recognizes revenue using the cost incurred to date as compared to the total estimated cost of each performance obligation. The impact on revenue of changes in total estimated costs are recognized on a cumulative basis in the period that the change occurs. If estimates of the total cost change, or if contract amendments change the scope of the performance obligation, the required adjustments to revenue could be material.

(ii) *Customer options* - The Company evaluates the customer options for material rights or options to acquire additional goods or services at no incremental consideration or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until the option is exercised and performance obligations are satisfied. If an option is not exercised before the option right expires, the Company will accelerate and recognize all remaining revenue related to the material right performance obligation.

(iii) *Research and development services* - The promises under the Company's collaboration agreement include research and development services to be performed by the Company for or on behalf of the customer. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts. Reimbursements are recognized in revenue in the Company's statements of operations and comprehensive loss. Expenses incurred as part of the Company's efforts to perform the research and development services are recognized in research and development expense in the Company's statements of operations and comprehensive loss.

(iv) *Manufacturing services* - The promises under the Company's collaboration agreement include manufacturing services to be provided by the Company. Payments or reimbursements resulting from the Company's manufacturing services are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts. Reimbursements are recognized in revenue in the Company's statements of operations and comprehensive loss. Expenses incurred to perform the manufacturing services are recognized in research and development expense in the Company's statements of operations and comprehensive loss.

(v) *Milestone payments* - At the inception of each arrangement that includes development or regulatory milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's, such as regulatory approvals, are not considered probable of being achieved until those approvals are received, and therefore, consideration included in the transaction price is constrained. The Company applied the variable consideration allocation exception under ASC 606 whereby variable milestone payments are not estimated and included in the transaction price at inception. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if

necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

(vi) *Commercial milestone payments and royalties* - For arrangements that include sales-based royalties, including milestone payments based on levels of sales, if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied)

Sale of Non-Financial Assets

Sale of non-financial assets that are outside the scope of the Company's ordinary activities are accounted for under ASC 610-20, *Other Income - Gains and Losses from the Derecognition of Non-financial Assets* ("ASC 610-20"). Pursuant to ASC 610-20, the Company applies the guidance in ASC 606, *Revenue from Contracts with Customers* ("ASC 606"), to determine if a contract exists, identify the distinct non-financial assets, and determine when control transfers and, therefore, when to derecognize the non-financial asset. Additionally, the Company applies the measurement principles of ASC 606 to determine the amount of consideration, if any, to include in the calculation of the gain or loss for the non-financial asset.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist primarily of employee-related costs, including salaries, benefits and stock-based compensation for employees engaged in research and development activities, costs related to research activities, preclinical studies and clinical trials, contract manufacturing for the production of clinical and preclinical materials, information technology-related costs, allocated overhead costs including facility-related expenses, consulting fees, costs related to laboratory operations and fees paid to other entities that conduct certain research and development activities on the Company's behalf. Payments made prior to the receipt of goods and services to be used in research and development are deferred and recognized as expense in the period in which the related goods are received or services are rendered.

The Company has entered into agreements with outsourced contract manufacturing and development and clinical research vendors. The Company estimates accrued research and development expenses as of each balance sheet date based on facts and circumstances known at that time. The Company periodically confirms the accuracy of its estimates with internal management personnel and external service providers, and makes adjustments, if necessary. Research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development services provided, but not yet invoiced, are included in accrued expenses on the balance sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered.

Patent Expenses

Costs to secure and maintain patents covering the Company's technology and product candidates are expensed as incurred and are classified as general and administrative expenses in the statements of operations and comprehensive loss.

Fair Value Measurements

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability 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. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Fair Value of Financial Instruments

The Company defines fair value as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities, which are required to be recorded at fair value, the Company considers the principal or most advantageous market in which to transact and the market-based risk. The carrying values of the Company's cash and cash equivalents, restricted cash, accounts receivable, accounts payable and accrued expenses, approximate their fair values due to their relatively short maturities.

Stock-Based Compensation

Stock-based compensation expense is recognized based on the grant-date fair value of the awards. The fair value of stock options and employee stock purchase plan ("ESPP") is determined using the Black-Scholes option pricing model on the date of grant. The fair value of restricted stock awards is determined using the estimated fair value of the Company's common stock on the date of grant.

Prior to the IPO, the Company utilized estimates and assumptions in determining the fair value of its common stock, including stock-based awards. The Company has granted stock options at exercise prices that represented the fair value of its common stock on the specific grant dates. The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately Held Company Equity Securities Issued as Compensation, to estimate the fair value of its common stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions, the prices at which the Company sold shares of convertible preferred stock, the superior rights and preferences of the convertible preferred stock senior to the Company's common stock at the time, and a probability analysis of various liquidity events, such as a public offering or sale of the Company, under differing scenarios.

For stock-based awards with service conditions only, the Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period, which is generally the vesting term of the award of four years. For stock-based awards with vesting criteria subject to the achievement of performance-based conditions, in addition to service conditions, the Company recognizes stock-based compensation expense on an accelerated basis over the vesting period when achievement of the performance criteria becomes probable.

Stock-based compensation expense is recorded within research and development and general and administrative expenses in the accompanying statements of operations and comprehensive loss based on the function to which the related services are provided. The Company recognizes stock-based compensation expense for the portion of awards that have vested. Forfeitures are accounted for as they occur.

Income Taxes

The Company utilizes the asset and liability approach to account for income taxes. Under this method, deferred income tax assets and liabilities are recorded based on the estimated future tax effects of differences between the financial statement and income tax basis of existing assets and liabilities. Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit carryforwards, using enacted tax rates expected to be in effect in the year in which the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions recognized in the financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. 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 interest and penalties.

Comprehensive Loss

Comprehensive loss is defined as a change in equity of a business enterprise during a period resulting from transactions from non-owner sources. The Company's other comprehensive income (loss) is comprised solely of unrealized gains or losses on marketable securities. The Company has not recorded any reclassifications from other comprehensive gains or losses to net loss during the years ended December 31, 2025 and 2024.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration of potential dilutive securities. Vested restricted stock is treated as outstanding for accounting purposes. Unvested restricted stock is not considered to be outstanding for purposes of the calculation of basic net loss per share. Diluted net loss per share is computed by dividing the net loss by the sum of the weighted-average number of common shares outstanding during the period plus the potential dilutive effects of potential dilutive shares outstanding during the period. Potential dilutive securities include stock options, unvested restricted stock, and ESPP shares. The dilutive effect of stock options, unvested restricted stock, and ESPP shares is computed using the treasury stock method. For all periods presented in a net loss position, diluted net loss per share is the same as basic net loss per share since the effect of including potential dilutive securities is anti-dilutive.

Recent Accounting Pronouncements

Recently Adopted Accounting Pronouncements

In September 2025, the FASB issued ASU No. 2025-07, *Derivatives and Hedging (Topic 815) and Revenue from Contracts with Customers (Topic 606)*. The guidance refines the scope of Topic 815 by clarifying which contracts are subject to derivative accounting and expand the scope exception for certain contracts not traded on an exchange to include contracts for which settlement is based on operations or activities specific to one of the parties to the contract. In addition, ASU 2025-07 is expected to reduce diversity in the accounting for share-based non-cash consideration from a customer for the transfer of goods or services, as well as provide investors with more comparable information and reduce accounting complexity and related reporting costs. Adoption of the amendment allows for either the prospective or modified retrospective application and is effective for annual periods beginning after December 15, 2026, with early adoption permitted. The Company early adopted this standard using the prospective method for the derivative scope refinement with the effective date of January 1, 2025. Prior to adoption, the Company did not have contracts that include are subject to derivative accounting and the adoption of the ASU did not have a material impact on its financial statements.

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, which enhances the transparency and decision usefulness of income tax disclosures. The standard is intended to improve income tax disclosures primarily related to the rate reconciliation and income taxes paid information. This update also includes certain other amendments to improve the effectiveness of income tax disclosures. The ASU is effective for fiscal years beginning after December 15, 2024, on a prospective basis. Early adoption and retrospective reporting are permitted. The company follows the provisions set forth in ASU No. 2023-09 on a prospective basis.

Recently Issued Accounting Pronouncements Not Yet Adopted

From time to time, new accounting pronouncements are issued by the FASB, under its ASC or other standard setting bodies, and adopted by the Company as of the specified date.

In July 2025, the FASB issued ASU No. 2025-05, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses for Accounts Receivable and Contract Assets*, which provides a practical expedient that assumes that current conditions as of the balance sheet date do not change for the remaining life of the asset in developing reasonable and supportable forecasts during the application of the current expected credit loss model for current accounts receivable and current contract assets arising from transactions under ASC 606. ASU 2025-05 is effective for fiscal years beginning after December 15, 2025 and interim reporting periods within those annual reporting periods. Early adoption is permitted. The Company is currently evaluating the impact of adopting ASU 2025-05.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, which requires the Company to disclose more detailed information about the types of expenses (including employee compensation, depreciation, and amortization) included in each relevant income statement expense caption. The ASU is effective for fiscal years beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption is permitted. The Company is currently evaluating the impact that this update will have on its disclosures.

Emerging Growth Company Status and Smaller Reporting Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act, until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

The Company is also a smaller reporting company as defined in the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The Company may continue to be a smaller reporting company even after it is no longer an emerging growth company. The Company may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as its voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of its second fiscal quarter, or its annual revenue is less than $100.0 million during the most recently completed fiscal year and its voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of its second fiscal quarter.

3. Balance Sheet Components

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following (in thousands):

	As of December 31, 2025	2024
Prepaid expenses	$ 4,622	$ 4,278
Interest receivable	3,384	953
Prepaid bonus	361	260
Other current assets	1,152	239
Prepaid expenses and other current assets	$ 9,519	$ 5,730

Property and Equipment, Net

Property and equipment, net consist of the following (in thousands):

	As of December 31, 2025	2024
Lab equipment	$ 6,339	$ 5,679
Furniture, fixtures, and office equipment	1,222	1,222
Leasehold improvements	717	717
Computer equipment	401	401
Construction in progress	107	—
Total property and equipment	8,786	8,019
Less: Accumulated depreciation and amortization	(4,352)	(2,929)
Property and equipment, net	$ 4,434	$ 5,090

Depreciation and amortization expense was $1.6 million and $1.4 million for the years ended December 31, 2025 and 2024, respectively.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following (in thousands):

	As of December 31, 2025	2024
Accrued compensation expense	$ 5,606	$ 4,129
Accrued research and development expense	5,179	2,888
Accrued general and administrative expense	915	703
Employee stock purchase plan liability	319	—
Other current liabilities	148	78
Accrued expenses and other current liabilities	$ 12,167	$ 7,798

4. Collaboration and Research Service Agreements

For the year ended December 31, 2025, the Company's revenue is comprised solely of arrangements with Novo and Vertex. For the year ended December 31, 2024, the Company's revenue was solely comprised of the arrangement with Vertex.

Novo Collaboration Agreement

On May 13, 2025, the Company entered into a Collaboration and License Agreement with Novo (the "Novo Collaboration Agreement"). Under the Novo Collaboration Agreement, the Company and Novo are exclusively collaborating to leverage the Company's proprietary Native Complex Platform™ to discover, develop and commercialize multiple potential oral small molecule therapies for metabolic-related diseases based on certain specified molecular targets.

Upon effectiveness of the Novo Collaboration Agreement on July 1, 2025, the Company and Novo have commenced four simultaneous research and development programs (each an "R&D Program"), each pursuing one or more Collaboration Targets (as defined in the Novo Collaboration Agreement) from discovery through development candidate selection. Subject to certain limitations, Novo also has a right to modify the research plan with the option to commence additional R&D Programs. Novo will reimburse the Company for 100% of the fully burdened costs arising from all research and development activities undertaken by the Company under the Novo Collaboration Agreement. After development candidate selection, beginning with investigational new drug-enabling activities, Novo will be responsible for all further global development and commercialization for each product candidate at its sole cost and expense unless the profit share option described below is exercised. Novo is also responsible for all commercialization costs subject to the Company's profit share option for up to one program under the Novo Collaboration Agreement. Pursuant to the terms of the Novo Collaboration Agreement, the Company will provide Novo with exclusive licenses to enable Novo to develop and commercialize products directed at the Collaboration Targets. The Company retains all other rights to its Native Complex Platform™ and all of the Company's other research and development programs.

Upon effectiveness of the Novo Collaboration Agreement, the Company received a one-time, non-refundable upfront payment of $195.0 million in July 2025, which was recorded as deferred revenue in its balance sheet. The Company is also eligible to receive up to approximately $498.0 million in research, development, regulatory, and commercial milestone payments for each R&D Program. In addition, the Company is entitled to escalating, tiered royalties ranging from mid to high single-digits based on global product sales on a country-by-country and product-by-product basis with respect to a R&D Program until the later of ten years after the date of first commercial sale of the first product in such R&D Program in such country, expiration of specified patent rights covering such product in such country or the expiration of specified regulatory exclusivity for the first product in such R&D Program in such country.

Under the Novo Collaboration Agreement, the Company has a one-time option to share in the global development costs and operating profits or losses (in lieu of milestones and royalties) with respect to one licensed product (the "Profit Share Option"), subject to certain terms, conditions and limitations. In the event that the Company chooses to exercise the Profit Share Option, it will be required to repay Novo all previously reimbursed developmental costs pertaining to that program at a predetermined multiple and reimburse Novo for a portion of the continued R&D costs incurred under the selected licensed product and will share in the profits resulting from the commercialization of the licensed product.

Unless earlier terminated, the term of the Novo Collaboration Agreement continues until expiration of the last royalty term for the applicable product in the applicable country. The Novo Collaboration Agreement is subject to customary termination provisions, including termination by a party for the other party's uncured, material breach. The Novo Collaboration Agreement also includes customary representations and warranties, covenants and indemnification obligations.

The Company concluded the Agreement is not within the scope of Accounting Standards Codification 808, *Collaborative Arrangements* as the Company does not share equally in the exposure to significant risk. Accordingly, the Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Novo, is a customer.

At commencement, the Company identified the several performance obligations within the Novo Collaboration Agreement, including research and development services on research targets, option rights held by Novo, license to use the Company's intellectual property to conduct research and development activities, and participation on the joint steering committee ("JSC"). At inception of the Novo Collaboration Agreement, the Company identified the following performance obligations:

(i) Four combined performance obligations comprised of the license, related research services, and participation of the JSC for the four R&D Programs;

(ii) Manufacturing services related to one of the R&D Programs; and

(iii) A material R&D Program modification right held by Novo.

The Company concluded that the license granted at contract inception is not distinct from the research services as the research services significantly modify the intellectual property underlying the license. As a result, for each R&D Program, the license has been combined with the research services and JSC participation into a single performance obligation, which is the combined performance obligation comprised of the license, related research services, and JSC participation.

In assessing whether the various options under the Novo Collaboration Agreement represent material rights, the Company considered the additional consideration the Company would be entitled to upon option exercise and the standalone selling price of the underlying goods and services. For the material right identified above, the Company concluded the option provided Novo with a discount that it otherwise would not have received.

The Company recognizes revenue related to the combined license and research services performance obligation and the manufacturing performance obligation over time using the input method. Under the input method, the extent of progress towards completion is measured based on the ratio of actual cost incurred to date to the total estimated cost at completion of the performance obligations, which the Company believes best measures its progress towards satisfying the performance obligations. A cost-based input method of revenue recognition requires management to make estimates of cost to complete the performance obligation. Judgment is required to evaluate assumptions related to cost estimates. The estimated standalone selling price for the material right was determined based on the estimated discount provided to Novo and the probability that Novo would exercise the option.

The following table presents revenue recognized, unrecognized transaction price, and estimated revenue expected to be recognized in the future as of December 31, 2025 (in thousands):

	Transaction Price
Combined license, research and manufacturing services	$ 247,846
Material right	41,190
Total transaction price[1]	$ 289,036
Revenue recognized[2]	(45,377)
Unrecognized transaction price as of December 31, 2025	$ 243,659

(1) Comprised of the allocation of the $195.0 million one-time, non-refundable upfront payment, of which $153.8 million was allocated to the four R&D programs and manufacturing services and $41.2 million was allocated to the material right and $94.0 million of variable consideration related to estimated research and manufacturing services for the four R&D Programs.

(2) Recorded within revenue in the statement of operations and comprehensive loss for the year ended December 31, 2025, comprised of $26.8 million recognized of the one-time, non-refundable upfront payment and $18.6 million variable considerations related to estimated research services for the four R&D Programs.

Amounts due to the Company for satisfying the revenue recognition criteria or that are contractually due based upon the terms of the Novo Collaboration Agreement are recorded as accounts receivable in the Company's balance sheets. Contract liabilities consist of amounts received prior to satisfying the revenue recognition criteria, which are recorded as deferred revenue in the Company's balance sheets.

The following table summarizes the changes in deferred revenue for the year ended December 31, 2025 (in thousands):

Balance at January 1, 2025	$ —
Deferred revenue	195,000
Recognized revenue	(26,814)
Balance at December 31, 2025[1]	$ 168,186

(1) Comprised of $62.3 million of deferred revenue, current and $105.9 million of deferred revenue, non-current, which is expected to be recognized over 3.5 years. As of December 31, 2025, all of the Company's performance obligations are outstanding.

The Company periodically assesses the probability of receiving payments from achieving the research and development, collaboration target, and regulatory milestones and includes the payment in the transaction price when they are deemed probable. Royalties and commercial sale milestones will be recognized when the subsequent sales occur based on the sales or usage-based royalty exception. The Company also periodically reassesses the probability of exercising Profit Share Option. As of December 31, 2025, none of the milestones were deemed probable and no royalty revenue has been recognized, and the Profit Share Option was deemed improbable with no amount recognized for repayment of reimbursements to Novo.

Vertex Asset Purchase and Research Service Agreement

Vertex Asset Purchase Agreement

In September 2023, the Company entered into an asset purchase agreement with Vertex, under which Vertex acquired an in-process research and development ("IPR&D") asset related to a GPCR program, including all intellectual property, materials, and compounds associated with the program (the "Vertex Asset Purchase Agreement"). The Vertex Asset Purchase Agreement also provided for a potential milestone payment payable to the Company contingent upon the achievement of a milestone event.

In July 2025, this milestone event was determined achieved and, as a result, the Company received a payment of $12.5 million in August 2025, which was recorded as a gain on sale of non-financial asset within total operating expenses in the Company's statements of operations and comprehensive loss for the year ended December 31, 2025. The Company will not receive any other payments related to this IPR&D asset.

Vertex Research Service Agreement

In conjunction with the Vertex Asset Purchase Agreement in September 2023, the Company entered into research service agreement with Vertex under which the Company agreed to perform certain exploratory research activities for Vertex (the "Vertex Research Service Agreement"). The Company recognized service revenue associated with the Vertex Research Service Agreement over the performance period of the research services as the services were provided in accordance with ASC 606. The Vertex Research Service Agreement expired in September 2025.

During the year ended December 31, 2025, the Company recorded revenue of $0.6 million related to research activities performed in connection with the Vertex Research Service Agreement. During the year ended December 31, 2024, the Company recorded revenue of $1.1 million related to research activities performed in connection with the Vertex Research Service Agreement.

5. Marketable Securities and Fair Value Measurements

The Company records marketable securities and cash equivalents at their estimated fair values, which are based on market prices from a variety of industry standard data providers and generally represent quoted prices for similar assets in active markets or have been derived from observable market data.

The fair value measurements of the Company's cash equivalents and marketable securities are identified at the following levels within the fair value hierarchy (in thousands):

	As of December 31, 2025			
		Fair Value Measurement		
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	$ 63,736	$ 63,736	$ —	$ —
Commercial paper	50,163	—	50,163	—
Corporate securities	2,190	—	2,190	—
Marketable securities, current:	—			
U.S. treasury securities	141,984	—	141,984	—
Commercial paper	67,784	—	67,784	—
Corporate securities	32,573	—	32,573	—
U.S. government agency securities	28,026	—	28,026	—
Marketable securities, non-current:	—			
U.S. treasury securities	117,632	—	117,632	—
Corporate securities	35,713	—	35,713	—
U.S. government agency securities	4,224	—	4,224	—
Total measured at fair value	$ 544,025	$ 63,736	$ 480,289	$ —

	As of December 31, 2024			
		Fair Value Measurement		
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	$ 141,779	$ 141,779	$ —	$ —
Commercial paper	82,527	—	82,527	—
U.S. government agency securities	8,059	—	8,059	—
Marketable securities, current:				
U.S. treasury securities	73,555	—	73,555	—
Commercial paper	23,487	—	23,487	—
U.S. government agency securities	14,193	—	14,193	—
Corporate securities	1,492	—	1,492	—
Marketable securities, non-current:				
U.S. treasury securities	65,406	—	65,406	—
U.S. government agency securities	2,514	—	2,514	—
Corporate securities	1,946	—	1,946	—
Total measured at fair value	$ 414,958	$ 141,779	$ 273,179	$ —

Marketable Securities

As of December 31, 2025, the Company's marketable securities consist of debt securities, including U.S. treasury and agency securities, corporate debt securities and commercial paper. These marketable securities are carried at fair value and are included in the tables above. The Company records an allowance for credit losses when unrealized losses are due to credit-related factors. At each reporting date, the Company evaluates securities with unrealized losses to determine whether such losses, if any, are due to credit-related factors. The Company evaluates, among others, whether the Company has the intention to sell any of these marketable securities and whether it is not more likely than not that the Company will be required to sell any of them before recovery of the amortized cost basis. Neither of these criteria were met at December 31, 2025. The credit ratings of the securities held remain of the highest quality. Moreover, the Company continues to receive payments of interest and principal as they become due, and the Company's expectation is that those payments will continue to be received timely. Based on this evaluation, as of December 31, 2025, the Company determined that unrealized losses of its marketable securities were primarily attributable to changes in interest rates and non-credit related factors. As such, no allowances for credit losses were recorded at December 31, 2025. The Company did not hold marketable securities at December 31, 2024.

Interest receivable as of December 31, 2025 and 2024 was $3.4 million and $1.0 million, respectively, and is recorded as a component of prepaid expenses and other current assets on the Company's balance sheets.

As of December 31, 2025, all marketable securities in an unrealized loss position had been in an unrealized loss position for less than 12 months. As of December 31, 2025, 44 marketable securities had been in an unrealized loss position for a period of less than 12 months.

As of December 31, 2025, the following table summarizes the amortized cost and the unrealized gains (losses) of the marketable securities presented within marketable securities, marketable securities, non-current and cash equivalents (in thousands).

	Remaining Contractual Maturity (in years)	Amortized Cost	Unrealized Gains	Unrealized Losses	Aggregate Estimated Fair Value
Commercial paper	Less than 1	$ 117,939	$ 17	$ (9)	$ 117,947
U.S. treasury securities	Less than 1	141,688	296	—	141,984
Corporate securities	Less than 1	34,755	14	(6)	34,763
U.S. government agency securities	Less than 1	27,992	34	—	28,026
Total maturity less than 1 year		322,374	361	(15)	322,720
U.S. treasury securities	1 to 2	117,376	257	(1)	117,632
Corporate securities	1 to 2	35,699	24	(10)	35,713
U.S. government agency securities	1 to 2	4,223	2	(1)	4,224
Total		$ 479,672	$ 644	$ (27)	$ 480,289

As of December 31, 2024, the following table summarizes the amortized cost and the unrealized gains (losses) of the marketable securities presented within marketable securities, marketable securities, non-current and cash equivalents (in thousands):

	Remaining Contractual Maturity (in years)	Amortized Cost	Unrealized Gains	Unrealized Losses	Aggregate Estimated Fair Value
Commercial paper	Less than 1	$ 106,017	$ 6	$ (9)	$ 106,014
U.S. treasury securities	Less than 1	73,511	44	—	73,555
U.S. government agency securities	Less than 1	22,245	10	(3)	22,252
Corporate securities	Less than 1	1,491	1	—	1,492
Total maturity less than 1 year		203,264	61	(12)	203,313
U.S. treasury securities	1 to 2	65,427	37	(58)	65,406
U.S. government agency securities	1 to 2	2,492	22	—	2,514
Corporate securities	1 to 2	1,940	7	(1)	1,946
Total		$ 273,123	$ 127	$ (71)	$ 273,179

As of December 31, 2025, the following table summarizes marketable securities in an unrealized loss position (in thousands):

	Remaining Contractual Maturity (in years)	Fair Value	Gross Unrealized Loss
Commercial paper	Less than 1	$ 57,503	$ (9)
Corporate securities	Less than 1	10,064	(6)
Total maturity less than 1 year		67,567	(15)
Corporate securities	1 to 2	17,484	(10)
U.S. treasury securities	1 to 2	4,009	(1)
U.S. government agency securities	1 to 2	3,389	(1)
Total		$ 92,449	$ (27)

6. Leases

Operating Leases

The Company leases office and research and development space at the Company's headquarters in South San Francisco, California under an operating lease. In April 2021, the Company entered into a lease for 12,560 square feet, set to expire in February 2023. In September 2022, the lease was amended to add 9,348 square feet, totaling 21,908 square feet (the "Original Leased Space"), also expiring in February 2023. In December 2022, the Company entered into another lease amendment to extend the term of the Original Leased Space and added 22,911 square feet (the "Additional Leased Space"). The Company took control of the Additional Leased Space in November 2023, at which point the Company vacated the Original Leased Space to allow the landlord to renovate it.

Renovation of the Original Leased Space was completed in July 2024. Upon completion of the renovation of the Original Leased Space, the lease of the Original Leased Space commenced, resulting in the total leased premises increasing to 44,819 square feet (the "Leased Space").

The lease term for the Leased Space expires in July 2032, with an option to extend the lease for eight additional years (the "Extension Option"). As of December 31, 2025 and 2024, it was not probable that the Company would exercise the Extension Option, therefore, it was excluded from the right-of-use asset and lease liability calculations.

During the year ended December 31, 2024, the Company recorded a $12.5 million operating lease right-of-use asset and operating lease liability upon completion of the renovations of the 21,908 square foot office and research and development space (the "Original Leased Space") as the Company occupied the property. These amounts are disclosed in the supplemental information of noncash activities on the statements of cash flows.

The Company is required to pay base rent plus its proportionate share of operating expenses, as defined in the applicable lease agreement on all of its leases. Variable lease payments related to operating expenses including utilities, maintenance costs and real estate taxes were $1.1 million and $0.7 million for the years ended December 31, 2025 and 2024, respectively.

Operating lease expenses, excluding variable lease payments, were $4.7 million and $3.5 million for the years ended December 31, 2025 and 2024, respectively. Short-term lease expense was not material for the periods presented. As of December 31, 2025 and 2024, the weighted average remaining lease term of the Leased Space was 6.6 and 7.6 years, respectively. The weighted average incremental borrowing rate used for the calculation of the present value of lease payments over the lease term was 11.34% for both the years ended December 31, 2025 and 2024.

The following table summarizes the expenses recognized and cash paid for the Leased Space (in thousands):

	Years Ended December 31,	
	2025	2024
Cash paid for operating lease liabilities	$ 4,469	$ 1,631
Operating lease costs	4,721	3,462
Short-term lease costs	1,035	644

As of December 31, 2025, future minimum rental payments for operating leases were as follows (in thousands):

As of December 31,	Future Payments
2026	$ 4,612
2027	4,760
2028	4,912
2029	5,070
2030	5,234
Thereafter	8,616
Total lease payments	33,204
Less: imputed interest	(9,579)
Total present value of operating lease liabilities	$ 23,625
Operating lease liabilities, current	$ 2,212
Operating lease liabilities, non-current	21,413
Total operating lease liabilities	$ 23,625

As of December 31, 2025 and 2024, the Company did not have any finance leases.

7. Commitments and Contingencies

Legal Proceedings

In the ordinary course of business, the Company may be subject to legal proceedings, claims and litigation, as the Company operates in an industry susceptible to patent or other legal claims. The Company accounts for estimated losses with respect to legal proceedings and claims when such losses are probable and estimable. Legal costs associated with these matters are expensed when incurred. The Company was not subject to any material legal proceedings as of December 31, 2025 and 2024, and the Company is not currently a party to any legal proceeding that, if determined adversely to the Company, in management's opinion, is currently expected to individually or in the aggregate have a material adverse effect on the Company's business, financial condition or results of operations taken as a whole.

Indemnifications

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. As permitted under Delaware law and in accordance with its bylaws, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is or was serving in such capacity. The Company is also party to indemnification agreements with its officers and directors.

The maximum potential amount of future payments that the Company could be required to make under these provisions is not determinable; however, the Company currently holds director and officer liability insurance. This insurance limits the Company's

exposure and may enable it to recover a portion of any future amounts paid. The Company is not currently aware of any indemnification claims. In addition, the Company believes that the fair value of any potential indemnification obligations is minimal. Accordingly, the Company did not record any liabilities associated with these indemnification rights and agreements as of December 31, 2025 and 2024.

8. Convertible Preferred Stock

Immediately prior to the closing of the Company's IPO in October 2024, the Company's outstanding convertible preferred stock automatically converted into 22,839,774 shares of common stock. Converted preferred stock outstanding as of the date of the IPO consisted of 196,657,452 shares. Each share of outstanding convertible preferred stock was converted into common stock at a ratio of 8.6103 convertible preferred shares to 1 common share. No shares of convertible preferred stock were authorized, issued or outstanding at December 31, 2025 and 2024.

In November 2021, the Company executed a Series A Convertible Preferred Stock financing arrangement that would provide financing of up to $100.0 million over an initial tranche and subsequent callable tranches through the issuance of up to 100.0 million shares of Series A Convertible Preferred Stock at an issuance price of $1.00 per share. In the initial tranche, the Company issued 45.0 million shares of Series A Convertible Preferred Stock for net proceeds of $44.7 million, of which $30.0 million was received in cash, net of issuance costs, and $14.7 million was for the conversion of the then outstanding convertible promissory notes plus accrued interest. The Series A Convertible Preferred Stock financing arrangement represented an equity financing, per the terms of the outstanding convertible promissory notes, and as such the unpaid principal and accrued interest outstanding of $14.7 million was converted into 14.7 million shares of Series A Convertible Preferred Stock. Additionally, in November 2022, the Company executed the second tranche and issued 30.0 million shares of Series A Convertible Preferred Stock and received net cash proceeds of $30.0 million.

In June 2023, the Company entered into a Series B Convertible Preferred Stock financing arrangement in which 121,657,452 shares of Series B Convertible Preferred Stock were authorized to be issued at an issuance price of $1.23297 per share over two tranches, for total proceeds of up to $150.0 million. In June 2023 and July 2023, the Company issued an aggregate of 60.8 million shares of Series B Convertible Preferred Stock at an issuance price of $1.23297 per share for net proceeds of $74.5 million related to the first tranche, with a potential second tranche of additional funding for up to $75.0 million based on approval of the Board of Directors and consent of the majority of the holders of the then-outstanding Series B Convertible Preferred Stock. The Series B Convertible Preferred Stock Purchase Agreement provides that, upon the fulfillment of certain conditions, each investor will purchase its pro rata portion of the shares to be issued in additional Series B Convertible Preferred Stock closings. Further, the Company agreed to sell, and issue said shares of Series B Convertible Preferred Stock on the same terms as the first tranche in the Purchase Agreement. The Company did not separately account for tranche purchase rights described above as they were not freestanding from the associated shares of convertible preferred stock.

In May 2024, the Company executed the second tranche of the Series B Convertible Preferred Stock financing arrangement and issued the remaining 60.8 million shares of Series B Convertible Preferred Stock for net proceeds of $74.9 million.

9. Common Stock

As of December 31, 2025 and 2024, the Company was authorized to issue 500.0 million shares of common stock, par value $0.001 per share.

In October 2024, the Company amended and restated its certificate of incorporation, which was filed immediately prior to the closing of its IPO and among other things, increased the number of shares of common stock authorized for issuance to 500.0 million shares of common stock.

In October 2024, the Company completed its IPO of its common stock. In connection with the Company's IPO, the Company issued and sold 18.4 million shares of its common stock, which included an additional 2.4 million shares of common stock that were issued to the underwriters pursuant to the full exercise of their option to purchase additional shares of common stock, at the public offering price of $18.00 per share. As a result, the Company received $302.8 million in net proceeds, after deducting underwriting discounts and commissions and other offering costs payable by the Company of $28.4 million.

The holders of common stock are entitled to dividends when and if declared by the board of directors. The board of directors has not declared any dividends and the Company has not paid any dividends. The holders of common stock are entitled to one vote per share on all matters to be voted upon by the stockholders.

The Company reserved the following shares of common stock, on an as-converted basis, for future issuance:

	As of December 31, 2025	2024
Options issued and outstanding	4,378,484	2,938,982
Shares reserved for future grants under 2024 Plan	4,257,640	3,743,915
Shares reserved for 2024 ESPP	251,211	369,402
	8,887,335	7,052,299

10. Stock-Based Compensation

2024 Stock Option and Incentive Plan

In October 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 Stock Option and Incentive Plan (the "2024 Plan") which became effective on October 25, 2024. The 2024 Plan allows for the issuance of equity-based incentive awards to the Company's officers, employees, directors and consultants.

The 2024 Plan provides that the number of shares reserved and available for issuance under the 2024 Plan will automatically increase on January 1, 2025 and each January 1 thereafter through January 1, 2034 by 5% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Company's compensation committee.

The 2024 Plan replaced the Septerna, Inc. 2021 Stock Option and Grant Plan (the "2021 Plan") as the Company's board of directors determined not to make additional awards under the 2021 Plan following the completion of the IPO. However, the 2021 Plan will continue to govern outstanding equity awards granted thereunder. The shares of common stock underlying any awards under the 2024 Plan and the 2021 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated (other than by exercise) will be added to the shares of the Company's common stock available for issuance under the 2024 Plan. 4.3 million and 3.7 million shares remained available for future issuance under the 2024 Plan as of December 31, 2025 and 2024, respectively.

Stock options are governed by stock option agreements between the Company and recipients of stock options. Incentive stock options and nonqualified stock options may be granted under the 2024 Plan at an exercise price of not less than 100% of the fair market value of the common stock on the date of grant, determined by the Compensation Committee of the board of directors. Options become exercisable and expire as determined by the Compensation Committee, provided that the term of the stock options may not exceed ten years from the date of grant.

2021 Stock Option and Grant Plan

In 2021, the Company adopted the 2021 Plan, which authorizes the Company to grant incentive stock options, non-qualified stock options, restricted stock awards, unrestricted stock awards and restricted stock units, to officers, employees, directors, consultants, or other key persons of the Company. The terms of the stock option and restricted stock agreements, including vesting requirements, are determined by the Board of Directors, subject to the provisions of the 2021 Plan. Stock option awards expire 10 years from the grant date, or as otherwise determined by the Board of Directors, or in the case of incentive stock options granted to 10% stockholders, the term is no more than 5 years from the grant date. Additionally, the Company granted and issued restricted stock awards and allowed the recipients to purchase the unvested restricted stock awards at par value per share. The shares issued for unvested restricted stock awards under the 2021 Plan are subject to repurchase by the Company at the original issuance price in the event of the holder's termination of its relationship with the Company. Consideration received for shares associated with the unvested restricted stock awards is initially recorded as a liability and subsequently reclassified into stockholders' equity as the related awards vest over the requisite service period.

No shares remained available for future issuance under the 2021 Plan as of December 31, 2025 and 2024 as the 2021 Plan was replaced by the 2024 Plan.

Restricted Stock Awards

The Company granted restricted stock awards from the 2021 Plan and from outside of its stock plans, under the terms of restricted stock purchase agreements and subscription agreements. Unvested shares are subject to repurchase by the Company upon the holder's termination of its relationship with the Company at the original purchase price. Consideration received for shares associated with the

unvested restricted stock awards is initially recorded as a liability and subsequently reclassified into stockholders' equity as the related awards vest.

The following summarizes restricted stock award activity:

	Number of Shares Outstanding	Weighted-Average Grant Date Fair Value Per Share
Balance at December 31, 2024	576,829	$ 2.62
Restricted stock awards vested	(442,993)	2.85
Restricted stock awards repurchased	(2,612)	3.30
Balance at December 31, 2025	131,224	1.81

The restricted stock awards generally include a service condition for vesting and vest over four years with a one-year cliff vesting and pro-rata monthly vesting thereafter, but some awards vest over different time periods. In addition, some restricted stock awards include vesting criteria subject to the achievement of performance-based conditions in addition to service conditions ("performance RSAs"). As of December 31, 2025, none of the outstanding and unvested performance RSAs were subject to achievement of performance-based criteria for vesting. The aggregate grant date fair value of shares vested during the year ended December 31, 2025 was $1.3 million. The remaining liability related to restricted stock awards as of December 31, 2025 was not material and was recorded in accrued expenses and other current liabilities on the balance sheet.

Stock Options

The following summarizes stock option activity under the 2024 Plan:

	Options Outstanding			
	Total Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2024	2,938,982	$ 4.64	9.11	$ 53,706
Granted	1,914,914	12.44		
Exercised	(268,188)	3.66		
Cancelled	(207,224)	7.70		
Outstanding as of December 31, 2025	4,378,484	7.97	8.79	87,194
Exercisable as of December 31, 2025	1,096,087	4.60	8.19	25,516

Stock options include a service condition for vesting and generally vest over four years. The aggregate intrinsic values of options outstanding and exercisable were calculated as the difference between the exercise price of the options and the closing market price of the Company's common stock as of December 31, 2025.

The aggregate grant date fair value of options that vested for the year ended December 31, 2025 was $4.9 million. The options granted in the year ended December 31, 2025 and 2024 had a weighted-average per share grant-date fair value of $9.58 and $6.65, respectively, and a total grant date fair value of $18.3 million and $13.1 million, respectively. The total intrinsic value of stock options exercised during the year ended December 31, 2025 was $2.2 million.

2024 Employee Stock Purchase Plan

In October 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 ESPP. The 2024 ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2026 and each January 1 thereafter through January 1, 2034, by the lesser of (i) 0.4 million shares of common stock, (ii) 1% of the outstanding number of shares

of common stock on the immediately preceding December 31, or (iii) such lesser number of shares of common stock as determined by the administrator of the 2024 ESPP.

The 2024 ESPP provides eligible employees with an opportunity to purchase common stock from the Company and to pay for their purchases through payroll deductions.

The offering periods begin on May 1 and November 1, will be twenty-four (24) months in duration and include four (4) purchase periods, each purchase period lasting six (6) months. The purchase price will be 85% of the fair market value per share of the Company's common stock on either the offering date, which is the first trading day of the offering period, or the purchase date, which is the last trading day of the purchase period, whichever is less. If the fair market value of a share of the Company's common stock on any purchase date within a particular offering period is less than the fair market value on the start date of that offering period, then the offering period will automatically terminate and the employees in that offering period will automatically be transferred and enrolled in a new offering period which will begin on the next day following such purchase date.

During the year ended December 31, 2025, the Company issued 118,191 shares at a weighted average share price of $6.07 per share. As of December 31, 2025, there were 0.3 million shares available for issuance under the 2024 ESPP.

Stock Option and ESPP Valuation

In determining the fair value of the stock options and ESPP granted, the Company uses the Black-Scholes option pricing model and assumptions discussed below. This model utilizes inputs that are subjective.

Expected Term — The expected term represents the period that the Company's stock options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company has very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants. The Company will continue to apply this process until a sufficient amount of historical information regarding employee exercise patterns and post-vesting employment termination behavior becomes available.

Expected Volatility — Due to the Company's limited operating history and lack of company-specific historical volatility as a public company, due to the Company's IPO in October 2024, or implied volatility as a private company, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period, where available, equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, life cycle stage and area of specialty.

Risk-free Interest Rate — The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the options.

Expected Dividend — The Company has never paid dividends on its common stock and does not anticipate paying dividends on its common stock in the near future. Therefore, the Company used an expected dividend yield of zero.

The weighted-average assumptions used to value employee and non-employee stock option awards granted during the years ended December 31, 2025 and 2024, using the Black-Scholes option pricing model, were as follows:

	Years Ended December 31,	
	2025	2024
Risk-free interest rate	3.98 %	3.83 %
Expected volatility	92.1 %	91.1 %
Expected term (years)	5.97	6.03
Expected dividend yield	— %	— %

The weighted-average assumptions used to value employee stock purchase plan shares granted during the year ended December 31, 2025, using the Black-Scholes option pricing model, were as follows:

	Year Ended December 31,
	2025
Risk-free interest rate	3.82 %
Expected volatility	86.53 %
Expected term (years)	1.22
Expected dividend yield	— %

Stock-based Compensation Expense

Stock-based compensation expense for restricted stock awards, stock options, and ESPP recognized in the Company's statements of operations and comprehensive loss is presented as follows (in thousands):

	Years Ended December 31,	
	2025	2024
Research and development expense	$ 4,087	$ 1,619
General and administrative expense	4,389	1,533
Total stock-based compensation expense	$ 8,476	$ 3,152

As of December 31, 2025, total unrecognized stock-based compensation expense related to unvested restricted stock awards, stock options, and ESPP was $24.5 million, which is expected to be recognized over a weighted-average period of 2.7 years.

11. Income Taxes

The components of the provision (benefit) for income taxes were as follows for the years ended December 31, 2025 and 2024 (in thousands):

	Years Ended December 31,	
	2025	2024
Current:		
Federal	$ 12	$ (7)
State	—	—
Total current	12	(7)
Deferred:		
Federal	—	(491)
State	—	—
Total deferred	—	(491)
Provision (benefit) for income taxes	$ 12	$ (498)

As discussed in Note 2, we adopted ASU 2023-09 on a prospective basis beginning with the year ended December 31, 2025. For the year ended December 31, 2025, the tax provision expense was not material. For the year ended December 31, 2024, the Company recorded income tax benefit of $0.5 million.

A reconciliation of the Company's effective tax rate to the statutory U.S. federal rate is as follows:

	Year Ended December 31, 2025	
	Amount	Percentage
U.S. federal taxes at statutory rate	$ (10,262)	21.0 %
State tax, net of federal benefit	—	—
Tax credits	(1,195)	2.5
Change in valuation allowance	9,972	(20.4)
Nontaxable or nondeductible items		
Stock based compensation	1,081	(2.2)
Permanent differences	56	(0.1)
Other	(2)	—
Changes in unrecognized tax benefits	359	(0.8)
Other	3	—
Provision for income taxes	$ 12	— %

	Year Ended December 31, 2024
U.S. federal taxes at statutory rate	21.0%
State tax, net of federal benefit	8.0
Stock compensation	(0.7)
Tax credits	1.5
Change in valuation allowance	(29.0)
Other	(0.1)
Total effective income tax rate	0.7%

Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The types of temporary differences that give rise to significant portions of the Company's deferred income tax assets and liabilities are set out below (in thousands):

	Years Ended December 31,	
	2025	2024
Net operating loss carryforwards	$ 14,149	$ 7,122
Research and development credits	5,318	4,102
Operating lease liabilities	5,620	7,129
Stock-based compensation	474	61
Accrued liabilities	1,319	1,163
Section 174 capitalized research and development costs	22,932	20,855
Total deferred tax assets before valuation allowance	49,812	40,432
Valuation allowance	(44,015)	(33,061)
Total deferred tax assets	5,797	7,371
Property and equipment	(683)	(766)
Operating lease right-of-use assets	(5,114)	(6,605)
Total deferred tax liabilities	(5,797)	(7,371)
Net deferred income tax liabilities	$ —	$ —

The Company has established a valuation allowance for the amount of deferred tax assets that are not more likely than not to be realized. Management considered all available evidence, both positive and negative, including but not limited to the Company's historical operating results, income or loss in recent periods, cumulative losses in recent years, forecasted earnings, future taxable income, and significant risk and uncertainty related to forecasts, and concluded the deferred tax assets are not more likely than not to be realized. The net change in the total valuation allowance for the years ended December 31, 2025 and 2024 was an increase of $11.0 million and $20.9 million, respectively.

As of December 31, 2025, the Company had $45.8 million of federal net operating loss carryforwards and $77.9 million of state net operating loss carryforwards, available to reduce future taxable income. The federal net operating loss carryforwards will carryforward indefinitely. The state net operating loss carryforwards will begin to expire in 2041, if not utilized.

As of December 31, 2025, the Company had federal research and development tax credits carryforward of $5.2 million and state research and development tax credits carryforward of $3.7 million, available to reduce future income taxes. The federal research and development tax credits will begin to expire in 2040 if not utilized. The state research and development tax credits have no expiration date.

Internal Revenue Code section 382 ("IRC Section 382") places a limitation (the "Section 382 Limitation") on the amount of taxable income that can be offset by net operating loss ("NOL") carryforwards after a change in control (generally greater than 50% change in ownership) of a loss corporation. California has similar rules. When an ownership change occurs, IRC Section 382 limits the use of NOLs and credits in subsequent periods based on the annual 382 limitations. The annual 382 limitations may limit the full use of available tax attributes in one year but the identified ownership changes may not result in expiration of tax attributes for use prior to expiration of their respective carryforward periods. The Company performed a Section 382 analysis through the year ended December 31, 2024 and determined there were ownership changes in 2021 and 2023. The ownership changes did not result in a reduction of its net operating loss or in its research and development credit carryforwards expiring unused.

A reconciliation of the beginning and ending unrecognized tax benefit amount is as follows (in thousands):

	Years Ended December 31,	
	2025	2024
Balance at the beginning of the year	$ 3,567	$ 2,529
Additions based on tax positions related to current year	620	998
Adjustment based on tax positions related to prior years	(42)	40
Balance at end of the year	$ 4,145	$ 3,567

The reversal of the uncertain tax benefits would not impact the Company's effective tax rate as the Company continues to maintain a full valuation allowance against its deferred tax assets.

The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. During the years ended December 31, 2025 and 2024, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits.

The Company files income taxes in the U.S. federal jurisdiction, the state of California and various other U.S. states. The Company is not currently under examination by income tax authorities in federal, state or other jurisdictions. All income tax returns will remain open for examination by the federal, state and foreign authorities for three or four years, from the date of utilization of any NOLs or credits.

12. Related Parties

Third Rock Ventures

During the year ended December 31, 2024, the Company issued a total of 12.4 million shares of its Series B Convertible Preferred Stock to Third Rock Ventures VI, L.P., a holder of more than 5% of the Company's outstanding capital stock, during the second tranche closing in May 2024, for cash proceeds of $15.3 million. These shares were converted to shares of the Company's common stock upon the consummation of its IPO in October 2024. No shares were issued during the year ended December 31, 2025.

In August 2021, the Company entered into a service agreement with Third Rock Ventures, LLC ("TRV"), a holder of more than 5% of the Company's outstanding capital stock, (the "TRV service agreement") under which TRV provides consulting services to the Company. For the year ended December 31, 2024, the Company recorded expense of $0.3 million for such services as general and administrative expenses in the Company's statements of operations and comprehensive loss. As of December 31, 2024, $0.1 million of expense related to TRV was recorded in accrued expenses and other current liabilities. There was no expense recorded in accrued expenses and other current liabilities and no outstanding accounts payable to TRV at December 31, 2025.

The Company's former interim Chief Medical Officer, and also a current member of the Company's board of directors, was designated to the Company's board of directors by TRV and is affiliated with TRV. He did not receive any cash compensation from the Company for his service as its interim Chief Medical Officer as his services were provided to the Company through the TRV service agreement.

Of the total fees the Company incurred under the TRV service agreement for the year ended December 31, 2024, $0.2 million was attributed to consulting services provided by the board member. Additionally, as compensation for his services as the Company's interim Chief Medical Officer, the Company granted him options to purchase 23,227 shares during the year ended December 31, 2024 at the exercise price of $2.76 per share. The board member ceased serving as interim Chief Medical Officer in September 2024.

In December 2024, the Company entered into a separate consulting agreement with the board member, under which he may provide up to $9,500 of consulting services per month, which are also provided to the Company through the TRV service agreement. For the year ended December 31, 2025, the Company recorded expense of $0.1 million for such consulting services. As of December 31, 2025, there was a minimal expense recorded in accrued expenses and other current liabilities and a minimal outstanding accounts payable to the board member.

RA Capital

During the year ended December 31, 2024, the Company issued a total of 12.2 million shares of its Series B Convertible Preferred Stock to entities affiliated with RA Capital Management, L.P. (collectively, "RA Capital"), which held more than 5% of the Company's outstanding capital stock, during the second tranche closing in May 2024, for total cash proceeds of $15.0 million. These shares were

converted to shares of the Company's common stock upon the consummation of its IPO in October 2024. No shares were issued during the year ended December 31, 2025.

Samsara BioCapital

During the year ended December 31, 2024, the Company issued a total of 4.3 million shares of its Series B Convertible Preferred Stock to Samsara BioCapital, L.P. (“Samsara BioCapital”), a holder of more than 5% of the Company’s outstanding capital stock, during the second tranche closing in May 2024, for cash proceeds of $5.2 million. These shares were converted to shares of the Company's common stock upon the consummation of its IPO in October 2024. No shares were issued during the year ended December 31, 2025.

13. Net Loss Per Share

The Company had 4,554,420 shares of potentially dilutive securities, comprised of 4,378,484 outstanding stock options, 131,224 unvested restricted stock awards subject to repurchase, and 44,712 shares issuable under the ESPP, not included in the calculation of diluted net loss per share for the year ended December 31, 2025 because to do so would be anti-dilutive.

14. Employee Retirement Benefit Plan

The Company maintains a 401(k) retirement savings plan (the "401(k) Plan") for its employees. The 401(k) Plan allows eligible employees to make contributions up to the maximum allowable by the Internal Revenue Service ("IRS"). For the years ended December 31, 2025 and 2024, the Company made matching contributions of and recorded contribution expenses of $0.5 million and $0.2 million, respectively.

15. Segment Information

The CODM assesses performance for the Company's operating segment and decides how to allocate resources based on the Company's available cash resources. Total operating expenses and net loss of the Company's operating segment are used to monitor budget versus actual results. The measure of segment assets is reported as total assets on the Company's balance sheet.

The CODM is regularly provided with the following significant segment expenses:

	Years Ended December 31,	
	2025	2024
Revenue	$ 45,951	$ 1,075
Employee-related expenses, excluding stock-based compensation	33,468	22,233
Stock-based compensation	8,476	3,152
External research and development expenses	53,519	32,786
External general and administrative expenses	8,856	6,511
Gain on sale of non-financial asset	(12,500)	—
Other segment expenses*	22,429	17,216
Total operating expenses	114,248	81,898
Loss from operations	(68,297)	(80,823)
Other income, net	19,430	8,527
Loss before provision (benefit) for income taxes	(48,867)	(72,296)
Provision (benefit) for income taxes	12	(498)
Net loss	$ (48,879)	$ (71,798)

(*) Other segment expenses include facility related and office costs, information technology costs, general laboratory costs, and other operating expenses.

As of December 31, 2025 and 2024, all of the Company's property and equipment was maintained in the U.S. For each of the years ended December 31, 2025 and 2024, the Company's revenue was generated from providing research services and was earned in the U.S.

16. Subsequent Events

On January 8, 2026, the Company appointed Mark A. Wilson as Chief Legal Officer.

SEPTERNA, INC.

CORPORATE AND OTHER INFORMATION

Board of Directors

Jeffrey Finer, M.D., Ph.D.
Chief Executive Officer and Director
Septerna, Inc.

Jeffrey Tong, Ph.D.
Partner
Third Rock Ventures, LLC

Bernard Coulie, M.D., Ph.D., M.B.A.
President, Chief Executive Officer and Director
Pliant Therapeutics, Inc.

Abraham Bassan, M.S.
Partner
Samsara BioCapital L.P.

Alan Ezekowitz, M.D., D.Phil.
Advisory Partner
Third Rock Ventures, LLC

Keith Gottesdiener, M.D.
Former President, Director and Chief Executive Officer
Prime Medicine, Inc.

Jake Simson, Ph.D.
Partner
RA Capital Management, L.P.

Shalini Sharp, M.B.A.
Former Executive Vice President and Chief Financial Officer
Ultragenyx Pharmaceutical Inc.

Executive Officers and Senior Management

Jeffrey Finer, M.D., Ph.D.
Director and Chief Executive Officer

Gil M. Labrucherie, CFA, J.D.
Chief Financial Officer

Liz Bhatt, M.S., M.B.A.
President and Chief Operating Officer

Jae B. Kim, M.D.
Chief Medical Officer

Samira Shaikhly
Chief People Officer

Mark Wilson, J.D.
Chief Legal Officer

Uwe Klein, Ph.D.
Senior Vice President, Biological Sciences

Daniel Long, D.Phil.
Senior Vice President, Drug Discovery

Principal Executive Offices

250 East Grand Avenue
South San Francisco, CA 94080

Independent Registered Public Accounting Firm

Ernst & Young LLP
San Mateo, California

Transfer Agent

Computershare Trust Company, N.A.
150 Royall Street
Canton, MA 02021

Investor Relations

Investor Relations
investors@septerna.com

Visit Our Website

www.septerna.com

Form 10-K

The Company's Annual Report on Form 10-K for the year ended December 31, 2025, as filed with the SEC on March 9, 2026, except for exhibits, is printed as part of this 2025 Annual Report.

Additional copies are available without charge upon written request. Please address all requests to:

Septerna, Inc.
Attention: Corporate Secretary
250 East Grand Avenue
South San Francisco, CA 94080