2023

Annual Report

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2023

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: 001-40928

Ventyx Biosciences, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**83-2996852**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
12790 El Camino Real, Suite 200 **San Diego, California**	**92130**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (760) 593-4832

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 $0.0001 per share	**VTYX**	**The Nasdaq Global Select Market**

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 ☒

The aggregate market value of the common stock held by non-affiliates of the registrant, based on the closing price of the shares of common stock on June 30, 2023, as reported by The Nasdaq Stock Global Select Market on such date, was approximately $1.3 billion. Shares of the registrant's common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant have been excluded from this computation. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of February 22, 2024, the registrant had 59,252,349 shares of common stock, $0.0001 par value per share, outstanding.

Documents Incorporated by Reference

Portions of the registrant's Definitive Proxy Statement relating to the Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's fiscal year ended December 31, 2023.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. All statements other than statements of historical facts included in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "ongoing," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words.

These forward-looking statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- our expectations regarding our product candidates and their related benefits;
- our beliefs regarding the perceived benefits and limitations of competing products, and the future of competing products and our industry;
- details regarding our strategic vision and product candidate pipeline;
- our beliefs regarding the success, cost and timing of our development activities and current and future clinical trials, including study design;
- the anticipated timing of releasing data for any current or future clinical trials;
- the anticipated timing of commencement, enrollment, and completion of any current or future clinical trials for our product candidates;
- the timing or likelihood of regulatory filings or other actions and related regulatory authority responses;
- the ability and willingness of third parties to engage in research and development activities on our behalf involving our product candidates, and our ability to leverage those activities;
- our expectations regarding the ease of administration associated with our product candidates;
- our expectations regarding the patient compatibility associated with our product candidates;
- our beliefs regarding the potential markets for our product candidates and our ability to serve those markets;
- the ability to obtain and maintain regulatory approval of any of our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our ability to commercialize any approved products;
- the rate and degree of market acceptance of approved products, if any;
- our ability to attract and retain key personnel;
- the accuracy of our estimates regarding our future revenue, operating expenses, capital requirements and needs for additional financing;
- our ability to obtain funding for our operations, including funding necessary to complete further development and any commercialization of our product candidates;

- our ability to obtain, maintain, protect and enforce intellectual property protection for our product candidates and not infringe, misappropriate or otherwise violate the intellectual property of others; and
- regulatory developments in the United States and foreign countries.

You should refer to Part I, Item 1A (Risk Factors) of this Annual Report for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate.

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

Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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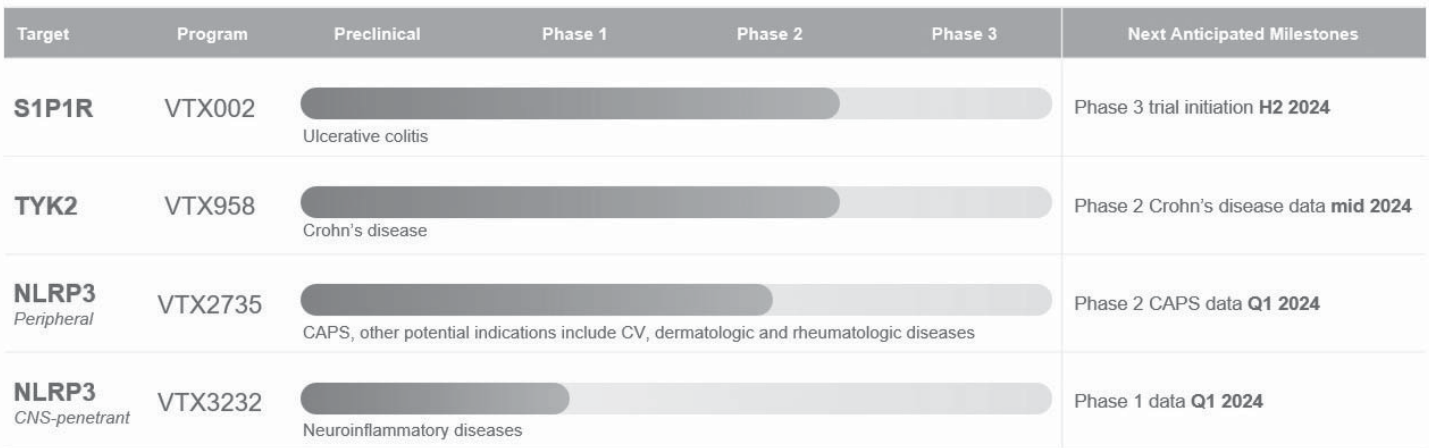
PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel small molecule product candidates to address a range of inflammatory diseases with significant unmet need. We leverage the substantial experience of our team in immunology to identify important new targets and to develop differentiated therapeutics against these targets. Our clinical product candidates address therapeutic indications with substantial commercial opportunity for novel small molecules. VTX002 is a sphingosine 1 phosphate receptor (S1P1R) modulator in development for patients with moderately to severely active ulcerative colitis (UC). During the fourth quarter of 2023, we reported positive topline results from a Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis. We expect to provide a data update from the open label extension period of the Phase 2 trial during the first quarter of 2024. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024. VTX958 is a selective allosteric tyrosine kinase type 2 (TYK2) inhibitor in Phase 2 development for the treatment of moderately to severely active Crohn's disease. We expect to report topline data from the Phase 2 trial of VTX958 in Crohn's disease during the middle of 2024. Our third product candidate, VTX2735, is a peripheral-targeted NOD-like receptor protein 3 (NLRP3) inflammasome inhibitor. We expect to announce topline results from a Phase 2 proof-of-concept trial for VTX2735 in cryopyrin-associated periodic syndrome (CAPS) patients during the first quarter of 2024. Our fourth product candidate, VTX3232, is a novel CNS-penetrant NLRP3 inhibitor in Phase 1 development. We expect to report results from a Phase 1 trial of VTX3232 in adult healthy volunteers during the first quarter of 2024.

Figure 1: Pipeline of current clinical programs



VTX002 (S1P1R Modulator)

VTX002 is an oral, selective peripherally restricted S1P1R modulator designed to have high selectivity for the S1P1 receptor. In a Phase 1 trial in healthy volunteers, VTX002 was well tolerated at all doses tested with no serious adverse events. In addition, VTX002 showed a dose-dependent and steady-state reduction in ALC of up to 65%. Reduction in circulating ALCs is recognized as a validated biomarker for efficacy in S1P1-mediated diseases, and S1P1 signaling has been identified as a key regulator of lymphocyte migration from lymph nodes into circulation. The blockade of this axis is a validated therapeutic approach in controlling aberrant leukocyte migration into the mucosa in inflammatory bowel disease ("IBD"). During the fourth quarter of 2023, we reported positive topline results from a Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis. We expect to provide a data update from the open label extension period of the Phase 2 trial during the first quarter of 2024. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024.

VTX958 (TYK2 Inhibitor)

VTX958 is an oral, selective allosteric inhibitor of TYK2, an intracellular signaling kinase in the JAK family. The JAK signal transduction and activator of transcription (STAT) signaling pathway is implicated in the pathogenesis of numerous inflammatory and autoimmune diseases. By inhibiting TYK2-mediated signal transduction, VTX958 has the potential to suppress chronic inflammation

while avoiding inhibition of other related members of the JAK family, such as JAK1, JAK2 and JAK3, thereby reducing the associated risk of infections and other side effects. In a Phase 1 single and multiple ascending dose clinical trial of VTX958 in healthy volunteers, VTX958 was well tolerated and demonstrated durable TYK2 target coverage as measured by target cytokines IL-12, IL-23 and IFNα. In the fourth quarter of 2023, we announced topline results from a Phase 2 trial of VTX958 in moderate to severe plaque psoriasis. While the trial achieved its primary endpoint, the degree of efficacy observed did not meet our internal threshold for advancement into Phase 3, leading to our decision to discontinue development of VTX958 in both plaque psoriasis and psoriatic arthritis.

We continue to evaluate VTX958 in a Phase 2 trial in patients with moderately to severely active Crohn's disease. In February 2024, we implemented a protocol amendment for the ongoing Phase 2 trial to streamline trial design and accelerate potential detection of an efficacy signal. As a result of the protocol amendment, target enrollment in the trial was revised from approximately 132 patients to approximately 93 patients. The trial's sole primary endpoint is now the change from baseline in the mean Crohn's disease activity index (CDAI) score at Week 12, while the proportion of patients achieving endoscopic response at Week 12 will be evaluated as a key secondary endpoint. We anticipate completing randomization of the trial during the first quarter of 2024 and expect to report topline results from the Phase 2 Crohn's disease trial during the middle of 2024.

VTX2735 and VTX3232 (NLRP3 Inhibitor Portfolio)

Inflammasomes are multi-protein complexes that sense molecular hallmarks of infection or cellular injury and initiate an appropriate immune response. We plan to harness the therapeutic potential of innate immune modulation with an initial focus on the NLRP3 inflammasome, one of the most widely studied members of the inflammasome family.

NLRP3 releases interleukin (IL)-1β when activated. Aberrant NLRP3 activation is implicated in a range of both acute and chronic inflammatory conditions. Although several biologics targeting the downstream cytokine IL-1β have been approved for treatment of autoimmune diseases (such as Cryopyrin-Associated Periodic Syndromes (CAPS), Familial Mediterranean Fever, Still's disease and juvenile idiopathic arthritis), we believe direct targeting of NLRP3 with an oral agent may have efficacy and safety advantages over these currently approved biologics.

VTX2735 is our lead peripherally-restricted NLRP3 inhibitor candidate. In June 2022, we announced positive topline data from a Phase 1 single and multiple ascending dose trial of VTX2735 in healthy volunteers, in which VTX2735 was well tolerated and demonstrated robust and durable inhibition of NLRP3 activity as measured by IL-1β. Based on these results, we initiated a Phase 2 proof-of-concept trial with VTX2735 in CAPS patients. We expect to announce topline results from the Phase 2 trial during the first quarter of 2024.

In addition to VTX2735, we are developing VTX3232, our lead CNS-penetrant NLRP3 inhibitor. We are conducting a Phase 1 single and multiple ascending dose trial of VTX3232 in healthy volunteers, and we expect to report topline results from this trial in the first quarter of 2024.

Our Competitive Strengths

We believe our drug discovery and development expertise has enabled us to identify and advance multiple small molecule product candidates from preclinical studies into clinical trials. Our extensive knowledge of the pathophysiology and biology of immunologic conditions informs our decision-making to advance the scientific and clinical path to demonstrate pharmacological activity and proof-of-concept, with the goal of achieving an efficient timeframe and cost-effective budget. The infrastructure within our discovery and development capabilities includes all aspects of the drug discovery process, such as medicinal and process chemistry, computational chemistry, structural biology, and *in vitro* and *in vivo* pharmacology. Our approach to drug discovery and development allows us to work in a seamless and simultaneous manner, rather than in sequential fashion. In our TYK2 inhibitor program, for example, we initiated our Phase 1 trial in March 2021, representing a 25-month timeframe from lead identification to a first-in-human trial.

The key elements of our approach to discovery and development include:

- An iterative lead optimization approach that utilizes rational and empirical drug design, allowing for advancement of our lead compounds and delivering drug candidates with high pre-clinical potency and selectivity for our immunology targets; and

- Relevant screening methods that utilize human cellular assays and human whole blood for our lead optimization assays, including a biomarker-driven approach. We believe that this approach offers the best and most relevant predictor of potency, efficacy and therapeutic window for our compounds in human clinical trials.

We have a diversified pipeline of product candidates, all of which we believe target large, well-established commercial markets. We intend to leverage our drug discovery and development approach and expertise to advance this pipeline, and to apply our knowledge of the immunology market to augment our pipeline through strategic partnerships.

Our Strategy

Our goal is to become a leader in developing differentiated product candidates for the immunology market and, ultimately, to address large, well-established commercial markets.

The three key elements to achieve this strategy include:

Focusing on the identification and development of differentiated product candidates against high value, validated immunology targets that address efficacy and safety limitations of currently approved drugs and those in development. Specifically, we intend to:

- **Advance VTX002, our selective S1P1R modulator through clinical development in UC.** VTX002 is an oral, selective peripherally restricted S1P1R modulator designed to have high selectivity for S1P1R. During the fourth quarter of 2023, we reported positive topline results from a Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis. We believe this trial may serve as the first of two pivotal trials required for registration. We expect to provide a data update from the open label extension period of the Phase 2 trial during the first quarter of 2024. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024.

- **Maximize the value of VTX958, our selective TYK2 inhibitor, in Crohn's disease.** Our oral TYK2 inhibitor, VTX958, is designed to have high selectivity for TYK2 without detectable inhibition of other JAK isoforms, potentially allowing VTX958 to avoid toxicities associated with these targets. We believe VTX958 may have the potential to become a first-in-class oral therapy for Crohn's disease. We expect to report topline results from the Phase 2 trial of VTX958 in Crohn's disease during the middle of 2024.

- **Advance our portfolio of NLRP3 inhibitors through early clinical development and proof-of-concept studies.** Our lead peripheral NLRP3 inhibitor, VTX2735, is an oral, selective small molecule inhibitor of NLRP3 that is designed for the treatment of systemic inflammatory diseases including cardiovascular, rheumatic, and dermatologic conditions. We are currently conducting a Phase 2 proof-of-concept trial with VTX2735 in CAPS patients. We expect to report topline results from the Phase 2 trial in the first quarter of 2024. In addition to VTX2735, we are developing VTX3232, a CNS-penetrant NLRP3 inhibitor, which we believe has potential therapeutic utility for the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and MS, among others. We are conducting a Phase 1 trial of VTX3232 in adult healthy volunteers, and we expect to report topline results from this trial in the first quarter of 2024.

Pursuing efficient and informed development of product candidates by fully leveraging the capabilities of our internal small molecule discovery engine and development infrastructure.

All of our pipeline candidates have been discovered and developed by members of our management team, each of whom has deep industry experience, while serving both at Ventyx and at companies that were later acquired by Ventyx (e.g., Oppilan Pharma Ltd. ("Oppilan") and Zomagen Biosciences Ltd. ("Zomagen")), including Dr. Raju Mohan, our chief executive officer. Our goal is to continue to leverage this infrastructure and expertise as we identify new, validated and high-priority inflammatory and immune disease candidates to continue building our pipeline portfolio and advancing new candidates through preclinical and into clinical development.

Entering into strategic partnerships that may expand our programs to maximize worldwide commercial potential of our product candidates.

All of our pipeline candidates have been discovered and developed by members of our management team while serving both at Ventyx and at companies that were later acquired by Ventyx (e.g., Oppilan and Zomagen). As a result, we currently hold worldwide rights to each product candidate. We may opportunistically evaluate and enter into strategic partnerships around certain product candidates, targets, geographies, or disease areas to expand the potential of our product candidates around the world.

Our Product Candidates

VTX002 (Sphingosine 1 Phosphate Receptor (S1P1R) Modulator)

Summary Overview of VTX002

VTX002 is an oral, selective, peripherally restricted S1P1R modulator designed to have high selectivity for the S1P1 receptor, which we are developing for the treatment of IBD. UC is our lead indication. S1P1 signaling has been identified as a key regulator of lymphocyte migration from lymph nodes into circulation. The blockade of this axis is a validated therapeutic approach to control aberrant leukocyte migration into the mucosa in IBD.

In a Phase 1 trial in healthy volunteers, VTX002 demonstrated a dose-dependent and steady-state reduction in absolute lymphocyte counts of up to 65%. Reduction in absolute lymphocyte counts is an established biomarker for S1P1-mediated pharmacodynamic effects that correlates with efficacy as demonstrated in multiple Phase 2 and Phase 3 trials conducted by third parties. VTX002 was well tolerated with no serious adverse events.

During the fourth quarter of 2023, we reported positive topline results from a Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis. We expect to provide a data update from the open label extension period of the Phase 2 trial during the first quarter of 2024. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024.

Overview of IBD

IBD is a complex disease with many contributing factors, including genetic, environmental and immunologic. Ulcerative colitis (UC) and Crohn's disease (CD) are the two most common forms of IBD. Both UC and CD are chronic, relapsing, remitting, inflammatory conditions of the GI tract that begin most commonly during adolescence and young adulthood. UC involves the innermost lining of the large intestine, and symptoms include abdominal pain and diarrhea, frequently with blood and mucus. CD can affect the entire thickness of the bowel wall and all parts of the GI tract from mouth to anus. CD symptoms include abdominal pain, diarrhea and other more systemic symptoms, such as weight loss, nutritional deficiencies and fever.

Overview of the IBD Market Opportunity

IBD is estimated to affect approximately 1,700,000 people in the U.S. and over 6,800,000 people globally. Incidence of IBD has been noted to be increasing in recent years, with CDC reports indicating that patients reporting as IBD sufferers has increased by up to 50% over the previous 15-20 years in the U.S. Approximately 30-40% of patients with IBD may be considered to have moderately to severely active disease and represent the target population for our drug candidates VTX958 (Crohn's disease) and VTX002 (ulcerative colitis).

In 2022, the IBD market for all levels of severity was approximately $24 billion globally, with the UC segment representing approximately $8 billion in 2022 sales and the CD segment representing approximately $16 billion in 2022 sales. The global IBD market share is currently majority-held by parenteral biologic agents. Market research suggests the IBD commercial market has significant growth potential driven by increasing disease incidence and the emergence of novel oral therapeutics, several of which have recently received regulatory approval or will seek regulatory approval in the coming years. We believe that the label expansion into UC for BMS' Zeposia, an S1P1R modulator, and the recent approval of Pfizer's S1P1R modulator, Velsipity, for UC will facilitate novel oral agents to increase their share of the UC market in future years. Meanwhile, the 2023 label expansion into CD for AbbVie's JAK inhibitor, Rinvoq, represents the first approval of an oral systemic therapy for moderately to severely active Crohn's disease, although the agent carries a "black box" warning for class-related safety risks. We believe projected gains for oral agents in IBD are supported by physician and patient general preference for oral administration over injectable biological therapies, high demand for new therapies with

competitive clinical profiles and the potential for potent and well-tolerated oral agents to expand the overall treated patient population in moderately to severely active IBD.

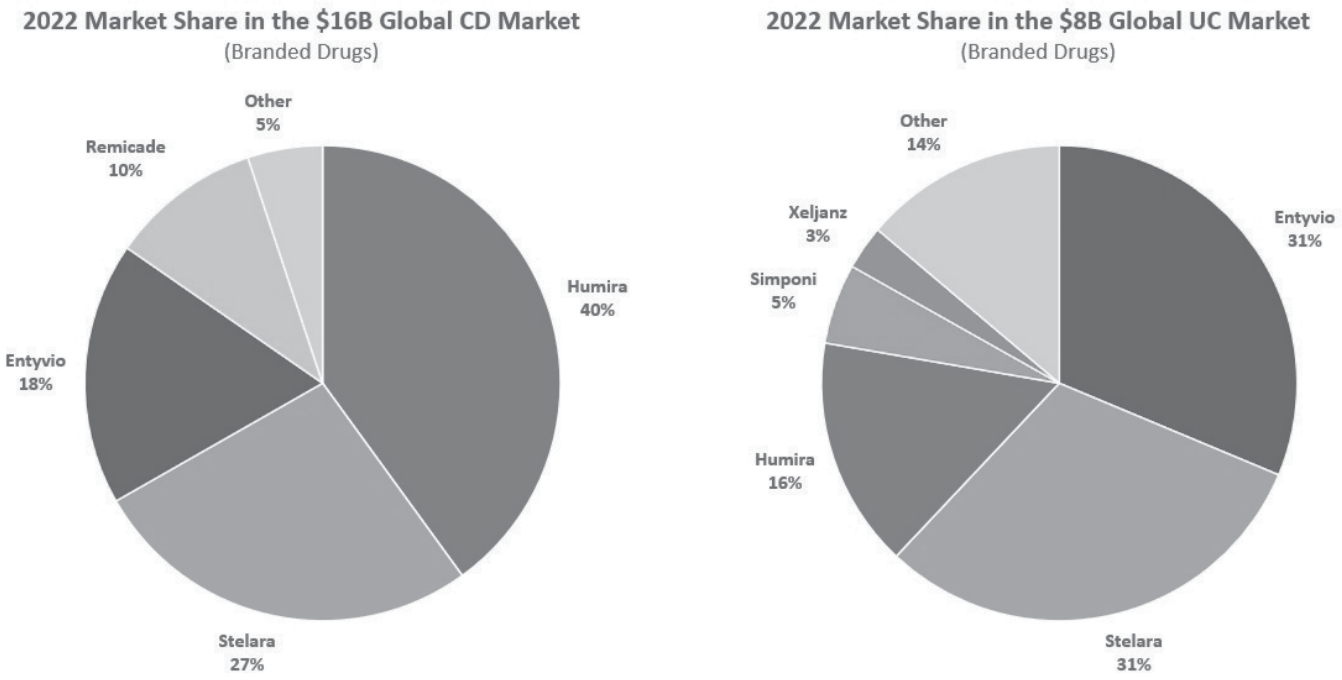
Treatment Paradigm in IBD

Mild-to-moderate IBD patients are commonly managed with 5-ASA (aminosalicylate) (mainly used in UC), corticosteroids or other immunosuppressive agents, including azathioprine and 6-mercaptopurine. Patients with a more serious initial disease presentation and those who have progressed or are intolerant of earlier line therapies frequently advance to biologic or novel oral medications (Figure 2). The mainstay biologics for treatment of moderately to severely active UC and/or CD are anti-TNFα biologics (including AbbVie's Humira, Johnson & Johnson's Remicade and Simponi, and UCB Pharma's Cimzia). Recently, treatment paradigms have begun shifting as additional options and more data become available with anti-integrin therapies (particularly Takeda's Entyvio) gaining traction in UC, and anti-IL-12/IL-23 and anti-IL-23 biologics (namely, Johnson & Johnson's Stelara and AbbVie's Skyrizi) frequently being used in CD. BMS' Zeposia, an S1P1R modulator, was approved for treatment of moderately to severely active UC in May 2021, and Pfizer's S1P1R modulator, Velsipity, was also approved for UC in October 2023. Pfizer's oral JAK inhibitor, Xeljanz, was approved for the treatment of UC in 2018, but commercial uptake has been limited due to its "black box" warning for risks, including serious infections, malignancy and thrombosis. AbbVie's Rinvoq, a next-generation oral JAK inhibitor, received FDA approval for moderately to severely active UC in March 2022, and for moderately to severely active CD in May 2023, but also carries a black box warning similar to other agents in the JAK class.

Despite available therapies, substantial unmet need remains as most approved therapies have generally failed to demonstrate a clinical remission effect size exceeding 10-15% relative to placebo in pivotal trials. Moreover, among those patients who do respond to therapy, up to 45-50% may lose response over time, owing to development of neutralizing antibodies or other issues. Modestly stronger remission rates have been reported recently, including in AbbVie's Phase 3 trials for JAK inhibitor Rinvoq (UC) and anti-IL-23 mAb Skyrizi (risankizumab-rzaa) (CD). These therapies have delivered effect sizes in the 20-30% range, but safety issues associated with the JAK inhibitor class and the need for injections with anti-IL-23 biologics may limit market share potential.

We believe there remains significant demand for well-tolerated and efficacious oral agents for the treatment of moderately to severely active CD and UC. According to studies, nearly half of patients taking biologic therapies may be expected to experience reduced efficacy over time leading to use of higher doses at substantially higher costs and elevated rates of drug discontinuation. Many moderately to severely active CD and UC patients refuse or are reluctant to adopt parenteral therapies, which, we believe, has contributed to a significant number of patients receiving sub-optimal care. The relapsing-remitting nature of IBD also may contribute to poor outcomes as patients may seek to discontinue therapies with undesirable or cumbersome administration during periods in which disease symptoms have abated.

Figure 2: Worldwide Market Share of Branded Drugs in Inflammatory Bowel Disease

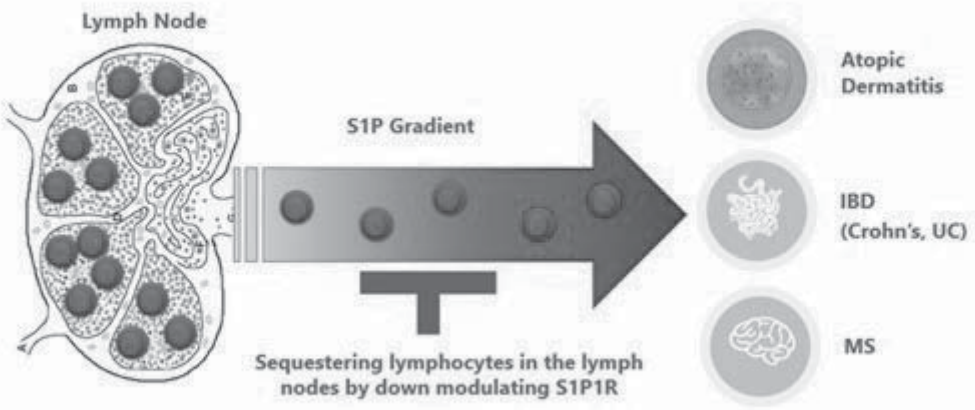


Rationale for Targeting S1P1R

S1P1R is a clinically validated target, as evidenced by the approval of BMS' Zeposia (ozanimod) for UC and multiple sclerosis (MS), Novartis' marketed therapies for MS, Mayzent (siponimod) and Gilenya (fingolimod), Johnson & Johnson's Ponvory (ponesimod) in MS, and, most recently, the FDA approval of Pfizer's Velsipity (etrasimod) for UC. S1P1R is a member of the sphingosine 1-phosphate receptor family of G protein coupled receptors (GPCRs). S1P1R is highly expressed on lymphocytes associated with the underlying inflammation of autoimmune diseases.

S1P1R modulation causes selective and reversible retention, or sequestration, of circulating white blood cells (lymphocytes) in peripheral lymphoid tissue (such as the lymph nodes) and in the thymus. The sequestration of lymphocytes is achieved by modulating cell migration patterns (known as lymphocyte trafficking), specifically preventing self-targeting, or autoreactive, lymphocyte migration to areas of disease inflammation, which is a major contributor to autoimmune diseases, including UC (Figure 3).

Figure 3: S1P1R modulation results in sequestration of lymphocytes, ameliorating lymphocyte-driven autoimmune diseases



Competition and Limitations of Current S1P1R Modulators for IBD

In May 2021, ozanimod became the first S1P1R modulator approved for the treatment of UC. In top-line results from a 645-patient, Phase 3 trial in UC, ozanimod showed moderate clinical efficacy with 18.4% of UC patients taking ozanimod achieving clinical remission compared to 6.0% of patients taking placebo. Currently, it is being studied in Phase 3 trials for the treatment of CD. In March 2022, Pfizer announced results of two Phase 3 trials with etrasimod in UC, demonstrating a placebo-adjusted clinical remission rate (induction) of 19.6% in one trial and 9.7% in the other. Etrasimod (Velsipity) was approved by the FDA for the treatment of UC in October 2023. Etrasimod is also in Phase 2 development for the treatment of CD. Most predecessor S1P1R modulator compounds were developed as treatments for MS and, thus, have high CNS penetration. We believe that this property may contribute to efficacy in MS, but is not desirable in IBD. The clinical safety and efficacy profile of these compounds may be limited by issues, such as hepatotoxicity; inability to dose to upper end of tolerated dose range and therefore suboptimal pharmacodynamic effect; longer half-life in humans (for compounds with active circulating metabolites, such as ozanimod); and heart rate effects (on-target first-dose reduction in heart rate, which can be mitigated by dose titration as we demonstrated in our Phase 1 trial).

Our Solution: VTX002

VTX002 is an oral, selective peripherally restricted S1P1R modulator designed to have high specificity for S1P1R with no detectable activity against the S1P2 and S1P3 receptors, which are associated with cardiovascular and pulmonary risks (Figure 4). VTX002 has very low CNS penetration and ocular distribution which, we believe, may reduce the risk of serious complications of S1P1 modulation in CNS, including macular edema.

Figure 4: VTX002 selectivity profile

S1P Receptor	S1P1R	S1P2R	S1P3R	S1P4R	S1P5R
EC_{50} (nM)	13	> 10,000	> 10,000	> 10,000	100

In our Phase 1 trial, VTX002 was well-tolerated with no serious adverse events or notable safety findings. In the therapeutic active dosing range tested, VTX002 showed dose-dependent steady-state reduction in absolute lymphocyte count of up to 65% which we believe is strongly predictive of likely clinical effect in UC and potentially other conditions. In addition, we established a dose titration schedule in the Phase 1 MAD trial to mitigate known first-dose heart rate effects associated with this class of drugs.

VTX002's wide therapeutic index allows us to explore the upper end of the dosing range, which may translate into clinical efficacy in certain indications. VTX002 has a half-life of 20 hours and no long-acting active metabolites, which enables a rapid onset of action and rapid recovery from pharmacologic activity compared to other agents, such as ozanimod.

Specifically, ozanimod's activity is achieved largely through circulating active metabolites, which can have an effective half-life of around 11 days (compared to a half-life of approximately 21 hours for ozanimod itself). This extended circulating half-life can lead to a slower time of onset of pharmacologic activity, which may result in a longer time to achieve maximal efficacy. In addition, the extended circulating half-life may introduce potential safety risk in the event of a serious infection because lymphocyte counts may take longer to rebound to normal circulating levels than with a shorter-acting agent, such as VTX002.

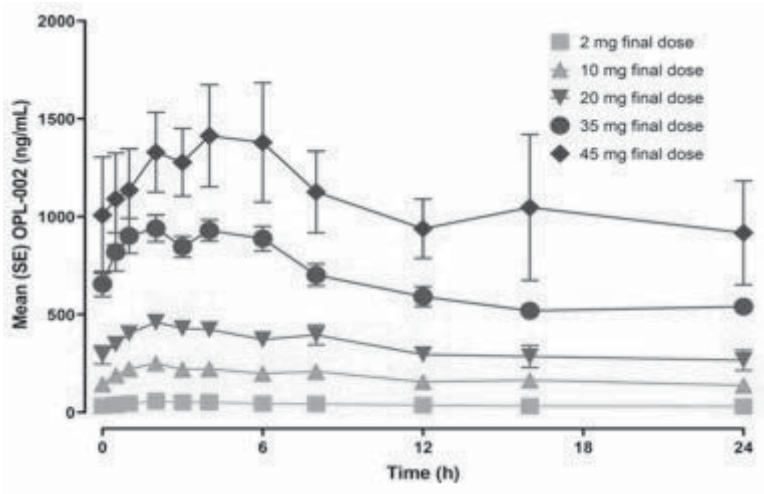
We believe VTX002 has the potential to be a modulator of S1P1R in multiple, large autoimmune diseases. In addition to UC and MS, S1P1R modulators have previously been evaluated through Phase 2 studies in CD.

Summary of VTX002 Phase 1 Clinical Data

In the Phase 1 double-blind, placebo-controlled SAD and MAD trials in 88 healthy volunteers, once-daily dosing of VTX002 was well tolerated for up to 28 days. The trials were designed to evaluate the safety, tolerability, dose-response, pharmacokinetics and pharmacodynamics of VTX002 compared to placebo. There were no serious adverse events reported. No subjects had liver function test elevations, pulmonary function or ocular exam abnormalities, or other notable safety findings, which have been seen with other S1P1R modulators.

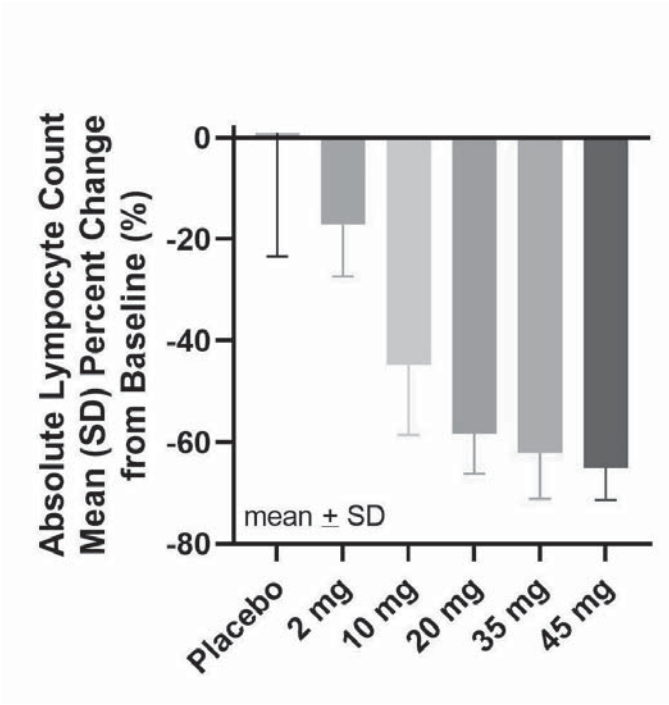
Once-daily dosing of VTX002 in the Phase 1 MAD trial demonstrated a half-life of approximately 20 hours and a dose-proportionate exposure after single and multiple doses of VTX002 with steady-state reached after 4 to 7 days of target-dose exposure.

Figure 5: Phase 1 MAD Results – Pharmacokinetics



In the Phase 1 MAD trial, once-daily dosing of VTX002 led to a dose-dependent steady state reduction in mean absolute lymphocyte count of up to 65% (Figure 6). Following the last dose of VTX002 in the MAD cohorts, lymphocyte counts started to return to normal within 72 hours.

Figure 6: Placebo adjusted lymphocyte count in MAD trial of VTX002

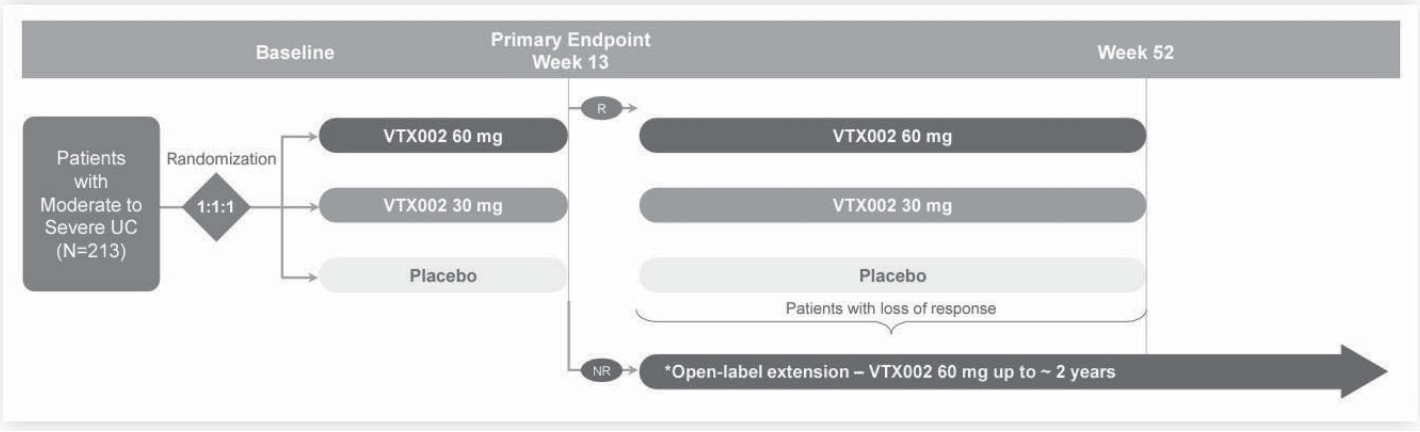


No clinically significant first-dose reduction in heart rate was observed following treatment with VTX002 at expected therapeutic dose levels following our 7-day titration schedule.

Summary of VTX002 Phase 2 Clinical Data in Ulcerative Colitis

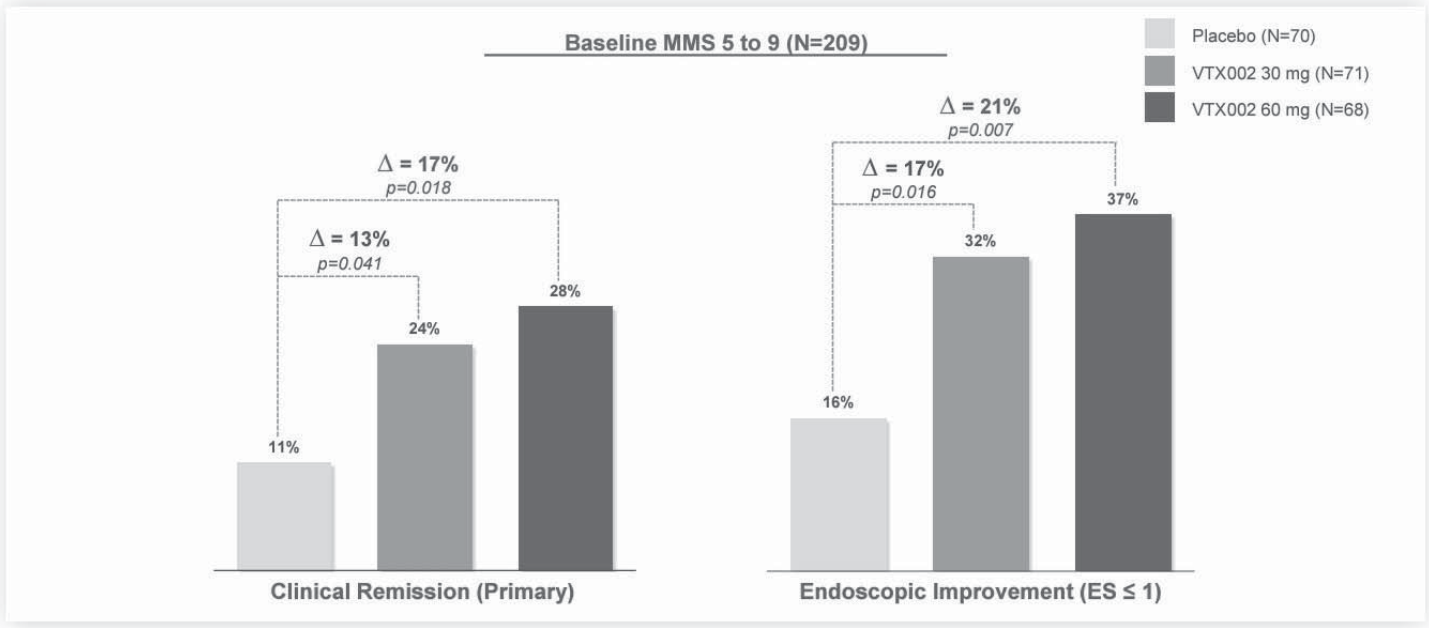
The Phase 2 trial of VTX002 was a 13-week, randomized, double-blind, placebo-controlled, dose-ranging trial evaluating the efficacy and safety of two oral doses of VTX002 (30 mg and 60 mg once daily) in patients with moderately to severely active UC. The primary endpoint was the proportion of patients achieving clinical remission at Week 13 as defined by the modified Mayo Clinic Score. Secondary endpoints included endoscopic, histologic, and symptomatic outcome measures.

Figure 7: Design of the VTX002 Phase 2 Trial in Ulcerative Colitis



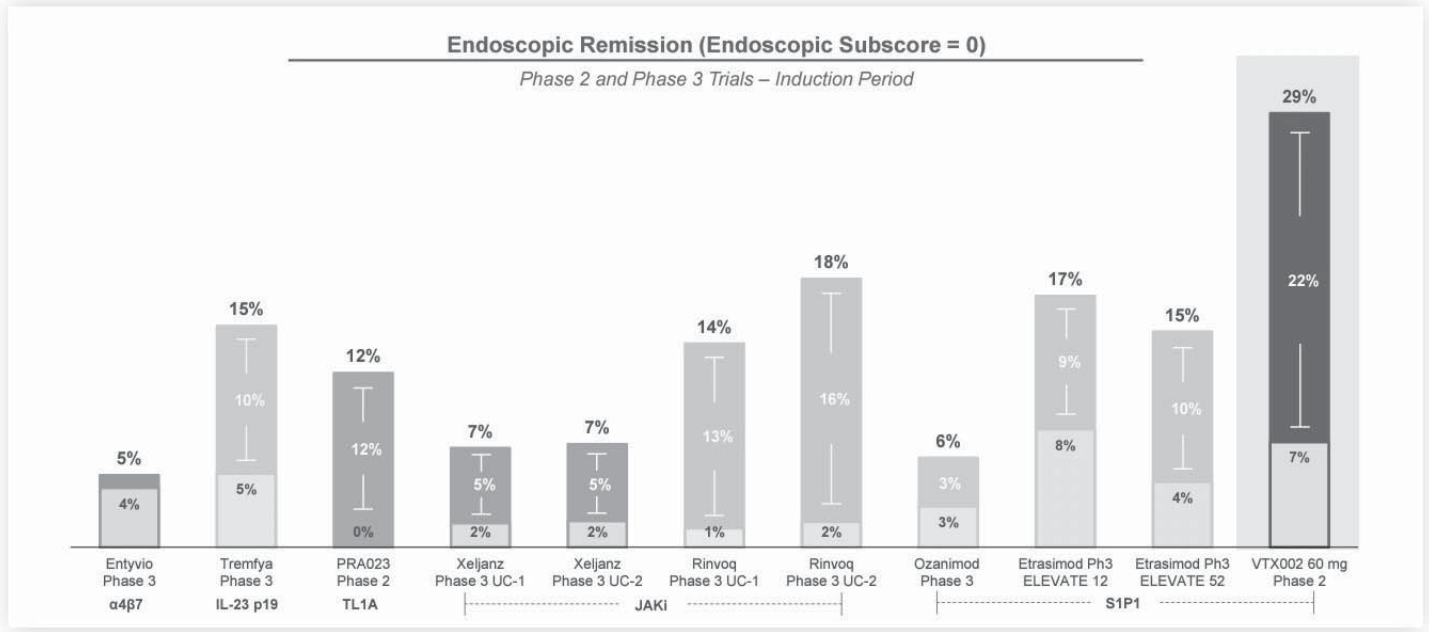
At week 13, 28% of patients on the VTX002 60 mg dose and 24% of patients on the VTX002 30 mg dose achieved the primary endpoint of clinical remission compared to 11% of patients on placebo. A strong, dose-dependent treatment effect was also observed on the secondary endpoint of endoscopic improvement (Mayo endoscopic subscore ≤1), with 37% of patients on VTX002 60 mg and 32% of patients on VTX002 30 mg achieving endoscopic improvement, compared to 16% of patients on placebo.

Figure 8: VTX002 Phase 2 Clinical Remission (Primary Endpoint) and Endoscopic Improvement Results



In addition to clinical remission and endoscopic improvement, treatment with VTX002 resulted in a high rate of complete endoscopic remission, defined as a Mayo endoscopic subscore of 0. Achievement of complete endoscopic remission is a consensus aspirational treatment goal that is associated with improved long-term patient outcomes. At week 13, 29% of patients on VTX002 60 mg and 21% of patients on VTX002 30 mg achieved complete endoscopic remission, compared to 7% of patients on placebo. We believe the high rate of endoscopic remission achieved by VTX002, combined with the highly competitive rate of clinical remission, underpins a potential best-in-class efficacy profile for an oral S1P1R modulator in moderately to severely active ulcerative colitis.

Figure 9: VTX002 Phase 2 Endoscopic Remission Results vs. Competitor Agents



VTX002 was well tolerated in both the 30 mg and 60 mg dose cohorts, with no treatment-related serious adverse events observed. There were no serious or opportunistic infections, and no instances of atrioventricular block, bradycardia, or macular edema were observed. We expect to present full results from the Phase 2 trial of VTX002 in ulcerative colitis at a future medical meeting.

Clinical Development Plan for VTX002

We believe the Phase 2 trial of VTX002 in UC may serve as the first of two pivotal trials required for registration. We expect to provide a data update from the open label extension period of the Phase 2 trial during the first quarter of 2024. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024.

VTX958 (Tyrosine Kinase Type 2 (TYK2) Inhibitor)

Summary Overview of VTX958

VTX958 is an oral, selective clinical-stage inhibitor of TYK2, an intracellular signaling kinase in the JAK family that regulates chronic inflammation in immune-mediated diseases. In preclinical studies, VTX958 inhibited only TYK2 and avoided inhibition of other related members of the JAK family (JAK1, JAK2, and JAK3). The inhibition of JAK1, JAK2, and JAK3 are associated with heightened risk of infections and other side effects. VTX958 has been designed to have a selectivity profile that positions it as a potential first-in-class therapeutic for the treatment of moderately to severely active Crohn's disease, a substantial commercial market.

In August 2022, we announced positive topline data from a Phase 1 single and multiple ascending dose trial of VTX958 in healthy volunteers, in which VTX958 was well tolerated and demonstrated durable TYK2 target coverage as measured by target cytokines IL-12, IL-23 and IFNα. In the fourth quarter of 2023, we announced topline results from a Phase 2 trial of VTX958 in moderate to severe plaque psoriasis. While the trial achieved its primary endpoint, the degree of efficacy observed did not meet our internal threshold for advancement into Phase 3, leading to our decision to discontinue development of VTX958 in both plaque psoriasis and psoriatic arthritis.

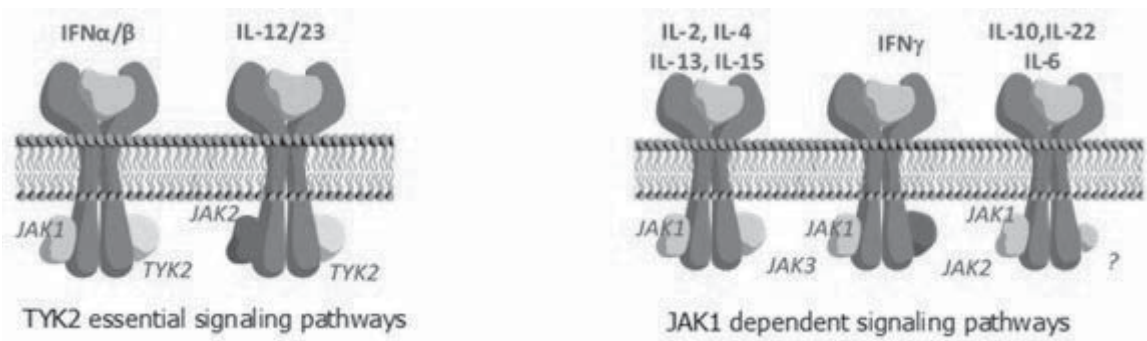
We continue to evaluate VTX958 in a Phase 2 trial in patients with moderately to severely active Crohn's disease. In February 2024, we implemented a protocol amendment for the ongoing Phase 2 trial to streamline trial design and accelerate potential detection of an efficacy signal. As a result of the protocol amendment, target enrollment in the trial was revised from approximately 132 patients to approximately 93 patients. The trial's sole primary endpoint is now the change from baseline in the mean Crohn's disease activity index (CDAI) score at Week 12, while the proportion of patients achieving endoscopic response at Week 12 will be evaluated as a key secondary endpoint. We anticipate completing randomization of the trial during the first quarter of 2024 and expect to report topline results from the Phase 2 Crohn's disease trial during the middle of 2024.

Oral TYK2 inhibitors, such as VTX958, inhibit the IL-12, IL-23 and Type I interferon pathways, which are modulated by biologic agents such as Ustekinumab (Stelara) and Risankizumab (Skyrizi). Thus far, these biologic agents are among the most effective in the treatment of moderately to severely active Crohn's disease. While newer biologics are typically regarded as safer than earlier-generation therapies, limitations include the need for injections, high cost of therapy, hypersensitivity reactions and long half-life in the case of an infection, providing an opportunity for safe and effective oral agents that target the same pathways.

Rationale for Targeting TYK2

The JAK-STAT (signal transducer and activator of transcription) DNA-binding pathways are required for molecular signaling of many cytokines that are important for the differentiation and effector functions of T helper cells, including, but not limited to, IL-12 and IL-23. There are four members of the JAK family—JAK1, JAK2, JAK3 and TYK2—all of which partner in cytokine receptor signaling.

Figure 10: Role of JAK family protein in cytokine receptor signaling pathways



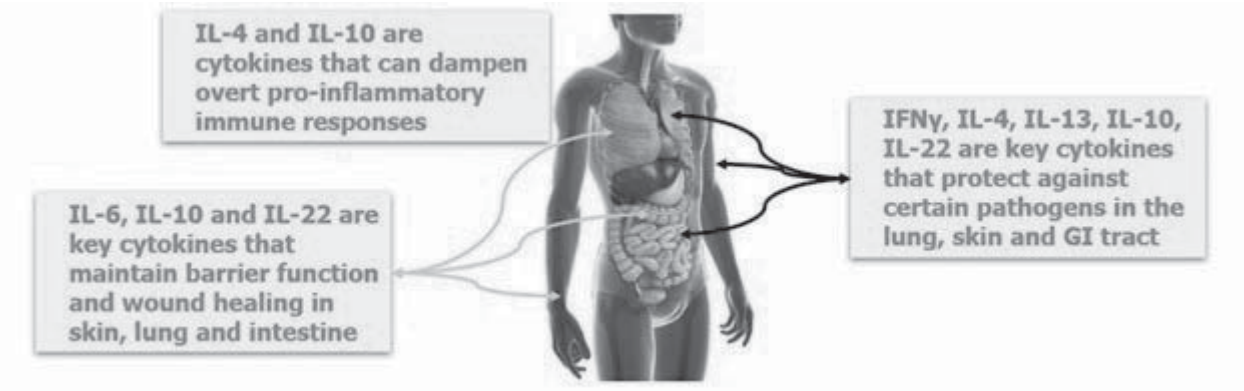
As shown in Figure 10, JAK kinases are associated with the intracellular domains of cytokine receptors and transduce receptor-mediated signals via JAK-STAT pathways. JAK1 has the broadest receptor specificity, with the ability to pair with all three other JAK family

members for signal transduction. JAK2 homodimers play an essential role in cytokines essential for hematopoietic homeostasis, such as GM-CSF and EPO signaling. JAK3 mainly pairs with JAK1 for signal transduction, while TYK2 pairs with either JAK1 for IFNα/β signaling or with JAK2 for IL-12/23 signaling.

Non-specific JAK inhibitors cause undesirable side effects due to the pleiotropic function of the cytokines they regulate. Inhibition of JAK1 affects a broad spectrum of immune functions, including: (1) the anti-inflammatory cytokines IL-4 and IL-10; (2) the IFNy pathway, which is important in pathogen defense; and (3) the cytokines IL-6, IL-10 and IL-22, which have important roles in maintaining mucosal barrier function. The most common serious treatment-related adverse event associated with JAK1 inhibitors is infection.

Inhibition of JAK2, which disrupts thrombopoiesis and hemopoiesis, is a major safety concern for first-generation JAK inhibitors. Second-generation JAK inhibitors that do not target JAK2, such as AbbVie's Rinvoq (upadacitinib) and Eli Lilly's Olumiant (baricitinib), have improved safety profiles, but safety concerns related to potential for toxicity related to JAK1 inhibition have contributed to black box product label warnings for these therapies from regulatory agencies.

Figure 11: Protective functions of cytokine pathways mediated by JAK1 that are spared by TYK2 inhibition



As shown in Figure 11, JAK1 regulates signaling downstream of many cytokines, including IFNy, IL-4, IL-6, IL-10, IL-13 and IL-22, which have protective functions.

We believe a highly selective TYK2 inhibitor with a potentially broad therapeutic window may be a powerful means by which to specifically address IFNα, IL-12 and IL-23-driven disease. Even though TYK2 is activated upon IL-6, IL-10 and IL-22 stimulation, it is essential only for IFNα/β, IL-12 and IL-23 signaling. We believe that a selective TYK2 inhibitor will affect only IFNα, IL-12 and IL-23 stimulated pathways, minimizing the safety concerns that likely arise from inhibition of other JAK kinases.

This hypothesis is supported by multiple genome-wide association studies that have identified human loss-of-function mutations in the TYK2 gene to be a protective factor in a variety of autoimmune diseases. Immune cells with these mutations are non-responsive to IFNα/β, IL-12 and IL-23 stimulation, but maintain normal responses to IL-10 and IL-6 stimulation. Importantly, individuals with loss-of-function mutations in the TYK2 gene are healthy, without increased risk of infection, indicating selective inhibition of TYK2 may present an optimal balance between reduction of autoimmunity and preservation of anti-pathogen immune function.

All JAK kinases contain a catalytic kinase domain (JH1), where critical phosphoryl transfer reactions responsible for STAT activation occur. All JAK kinases have a second, regulatory pseudokinase domain (JH2), which is autoinhibitory and functions to maintain the kinase domain in an inactive stand-by mode until an appropriate activation signal is received. The kinase domains of JAK family members are highly conserved, making the design of selective inhibitors targeting the established kinase function challenging. The regulatory JH2 domains of the JAK kinases, however, are much less conserved and have structurally distinct binding pockets, making them attractive targets for inhibitor design. Therefore, we have chosen to exploit these structural differences to design selective allosteric TYK2 inhibitors, typified by VTX958, which bind with high specificity to the JH2 domain of TYK2 and inhibit the kinase via disruption of its essential regulatory role in the signal transduction of TYK2.

Designing selective JAK inhibitors that directly and specifically inhibit the intended kinase function is challenging due to the structural similarity between kinase domain (JH1) ATP binding pockets of JAK family members. Allosteric inhibitors that bind to the regulatory pseudokinase JH2 domain have better selectivity for TYK2, but high homology between the JAK1 and TYK2 JH2 domains remains a challenge in designing selective agents. For example, while BMS's FDA-approved TYK2 inhibitor, Sotyktu, is a binder to the TYK2 JH2 domain, it also shows sub-nanomolar potency in a JAK1-JH2 binding assay. This interaction with the JAK1-JH2 pathway is

reflected in downstream signaling in IL-10 and IL-6 stimulation assays. We believe that less selective TYK2 inhibitors may produce toxicity arising from off-target effects when used at higher doses. Moreover, dose constraints on less selective compounds may result in sub-optimal inhibition of key pathways (i.e., IL-12, IL-23) that are relevant to targeting autoimmune conditions, such as Crohn's disease, in which high levels of target cytokine suppression may be required to achieve efficacy.

Our Solution: VTX958

VTX958 is an oral, selective allosteric inhibitor of TYK2 with a selective profile for TYK2 over other members of the JAK family. VTX958 was designed to inhibit IL-12, IL-23 and Type 1 interferon (IFNα/β) by binding selectively to the pseudokinase JH2 regulatory domain of TYK2, without inhibiting the analogous domains of JAK1, JAK2, or JAK3.

We believe that TYK2 inhibitors represent a new class of oral drugs that target pathways only partially addressed by current IL-12/IL-23 biologic therapies. A selective allosteric TYK2 inhibitor may play a critical role in offering a well-balanced therapy that: (1) mitigates harmful immune responses in these diseases while preserving protective immunity against pathogens; (2) avoids risk of injection-related reactions, including hypersensitivity; (3) overcomes patient reluctance to injections, thus potentially minimizing discontinuation rates; and (4) may be better positioned to address the cost and access limitations frequently associated with biologic therapies.

Table 1a: Binding of VTX958 to JH2 domains vs. Sotyktu (Ventyx data)

	VTX958	**SOTYKTU**
TYK2-JH2 Binding Kd	0.058 nM	0.009 nM
JAK1-JH2 Binding Kd	240nM	0.43 nM
Selectivity (fold)	>4,000	48

We have internally conducted pseudokinase domain binding assays comparing VTX958 and Sotyktu and have demonstrated that VTX958 has > 4,000-fold selectivity for its binding to the TYK2 JH2 domain as compared to its binding to the JAK1 JH2 domain. Sotyktu, by comparison, has high affinity for both TYK2 JH2 and JAK1 JH2 domains, binding with sub-nanomolar affinity to both domains with 48-fold selectivity. Our internal studies showed that VTX958 is approximately 80-fold more selective compared to Sotyktu in its binding affinity for the TYK2 JH2-allosteric domain (Table 1a) and we believe that this selectivity is also reflected in the high selectivity of VTX958 for TYK2 in cellular cytokine assays.

Table 1b: Cellular potencies of VTX958 (Ventyx data)

PRIMARY DRIVER	**CYTOKINE/CELL SYSTEM**	**VTX958 IC_{50}**
TYK2 Pathways	IFNα PBMC	12 nM
	IL-12 PBMC	35 nM
	IL-23 PBMC	5 nM
JAK1 Pathways	IL-22 PBMC	>10,000 nM
	IL-10 PBMC	>10,000 nM
	IFNγ PBMC	>10,000 nM
	IL-4 PBMC	>10,000 nM
	IL-6 PBMC	>10,000 nM

VTX958 shows high selectivity for TYK2-mediated cytokine pathways over JAK1-mediated pathways in multiple cellular cytokine stimulation assays conducted in both peripheral blood mononuclear cells (PBMCs), as shown in Table 1b, and in human whole blood (WB). Importantly, VTX958 was shown to have no detectable effect on JAK1-driven cytokines, including IL-6 and IL-10.

Phase 1 Trial of VTX958 in Healthy Volunteers

Overview

The Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) trial of VTX958 was a two-part, randomized, double-blind, placebo-controlled dose-escalation study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics

(PD) of single and multiple ascending doses. The study enrolled 96 adult healthy volunteers across SAD cohorts up to 500 mg and MAD cohorts up to 350 mg BID (twice a day) daily for 14 days.

Safety and Tolerability

VTX958 was well tolerated across all seven cohorts in the SAD portion and all five cohorts in the MAD portion of the Phase 1 trial with no discontinuations due to adverse events (AEs). No drug-related serious adverse events (SAEs) were reported. All treatment emergent adverse events (TEAEs) were classified as mild. No dose-limiting toxicities were identified and no dose-dependent trend in the frequency of TEAEs was observed. Additionally, there were no significant effects on hematological parameters, lipids/triglycerides and CPK laboratory values.

Exposure and Target Coverage

In both the SAD and the MAD portions of the trial, a dose-dependent increase in exposure was observed through all cohorts. In the MAD portion of the trial, VTX958 achieved TYK2 IC_{50} and IC_{90} coverage for up to 24 hours. The exposures achieved by VTX958 demonstrated potential class-leading coverage of TYK2 IC_{50} and IC_{90} and its target cytokines, IL-12, IL-23 and IFNα.

Figure 12: Exposure and Target Coverage Across All MAD Cohorts at Day 10

MAD Dose	Target Coverage* (hours)					
	IL-12		IL-23		IFNα	
	IC_{90}	IC_{50}	IC_{90}	IC_{50}	IC_{90}	IC_{50}
50 mg BID	0	5	0	5	0	7
250 mg QD	4	9	4	9	6	10
500 mg QD	6	14	6	14	7	16
175 mg BID	**16**	**24**	**16**	**24**	**17**	**24**
350 mg BID	**24**	**24**	**24**	**24**	**24**	**24**

*Data from Phase 1 MAD Day 10 (steady state); exposures used for target coverage calculations:

- IL-12 hWB IC_{90} = 865 ng/mL; IC_{50} = 130 ng/mL; IFNα hWB IC_{90} = 584 ng/mL; IC_{50} = 73 ng/mL
- IL-12 IC_{50} and IC_{90} values used for IL-23 IC_{50} and IC_{90} calibration (hWB assay not available for IL-23)
- IL-12 and IL-23 share TYK2-specific heterodimer IL-12Rβ1

Clinical Development Plan for VTX958

Based on these positive Phase 1 results, we advanced VTX958 into Phase 2 trials in psoriasis, psoriatic arthritis and Crohn's disease. In the fourth quarter of 2023, we announced topline results from a Phase 2 trial of VTX958 in moderate to severe plaque psoriasis. While the trial achieved its primary endpoint, the degree of efficacy observed did not meet our internal threshold for advancement into Phase 3, leading to our decision to discontinue development of VTX958 in both plaque psoriasis and psoriatic arthritis.

We continue to evaluate VTX958 in a Phase 2 trial in patients with moderately to severely active Crohn's disease. In February 2024, we implemented a protocol amendment for the ongoing Phase 2 trial to streamline trial design and accelerate potential detection of an efficacy signal. As a result of the protocol amendment, target enrollment in the trial was revised from approximately 132 patients to approximately 93 patients. The trial's sole primary endpoint is now the change from baseline in the mean Crohn's disease activity index

(CDAI) score at Week 12, while the proportion of patients achieving endoscopic response at Week 12 will be evaluated as a key secondary endpoint. We anticipate completing randomization of the trial during the first quarter of 2024 and expect to report topline results from the Phase 2 Crohn's disease trial during the middle of 2024.

VTX2735 and VTX3232 (NLRP3 Inhibitor Portfolio)

NLRP3 Inhibitor Portfolio

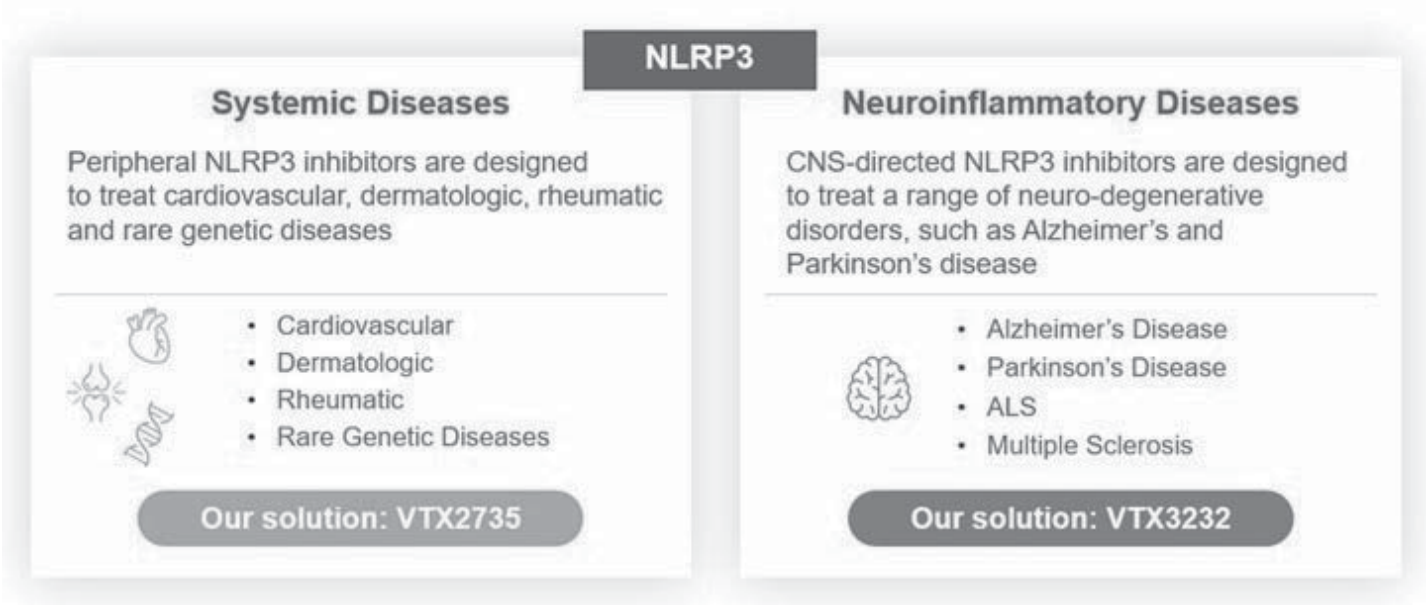
We have multiple programs focused on inhibitors of inflammasomes, multi-protein complexes that sense molecular hallmarks of infection or cellular injury and initiate an appropriate immune response. Inflammasomes have been recognized for their crucial role in host defense against pathogens, but dysregulated inflammasome activation is linked to the development of autoimmune, metabolic and neurodegenerative diseases, implicating them in a broad range of inflammatory diseases. These include systemic (i.e., cardiovascular (CV), dermatologic and rheumatic) diseases and CNS diseases (i.e., Alzheimer's disease, Parkinson's disease, multiple sclerosis, and others) (Figure 13).

We plan to harness the therapeutic potential of innate immune modulation, with an initial focus on the NLRP3 inflammasome. NLRP3 is the most widely studied member of the inflammasome family with the broadest role in autoimmune dysregulation and thus a high-value target for the treatment of multiple anti-inflammatory diseases.

We are developing a comprehensive portfolio of differentiated NLRP3 inhibitors to address multiple indications driven by aberrant NLRP3 activation. VTX2735 is our lead peripherally restricted NLRP3 inhibitor. We previously conducted a Phase 1 trial for VTX2735 in adult healthy volunteers, in which VTX2735 was well tolerated and demonstrated robust and durable inhibition of NLRP3 activity as measured by IL-1β. Based on these results, we initiated a Phase 2 proof-of-concept trial with VTX2735 in CAPS patients. We expect to announce topline results from the Phase 2 trial during the first quarter of 2024.

In addition to VTX2735, we are also developing VTX3232, a novel CNS-penetrant NRLP3 inhibitor. We are currently conducting a Phase 1 trial of VTX3232 in adult healthy volunteers. We expect to report topline results from the Phase 1 trial of VTX3232 during the first quarter of 2024.

Figure 13: Potential indications for NLRP3 inflammasome inhibitors

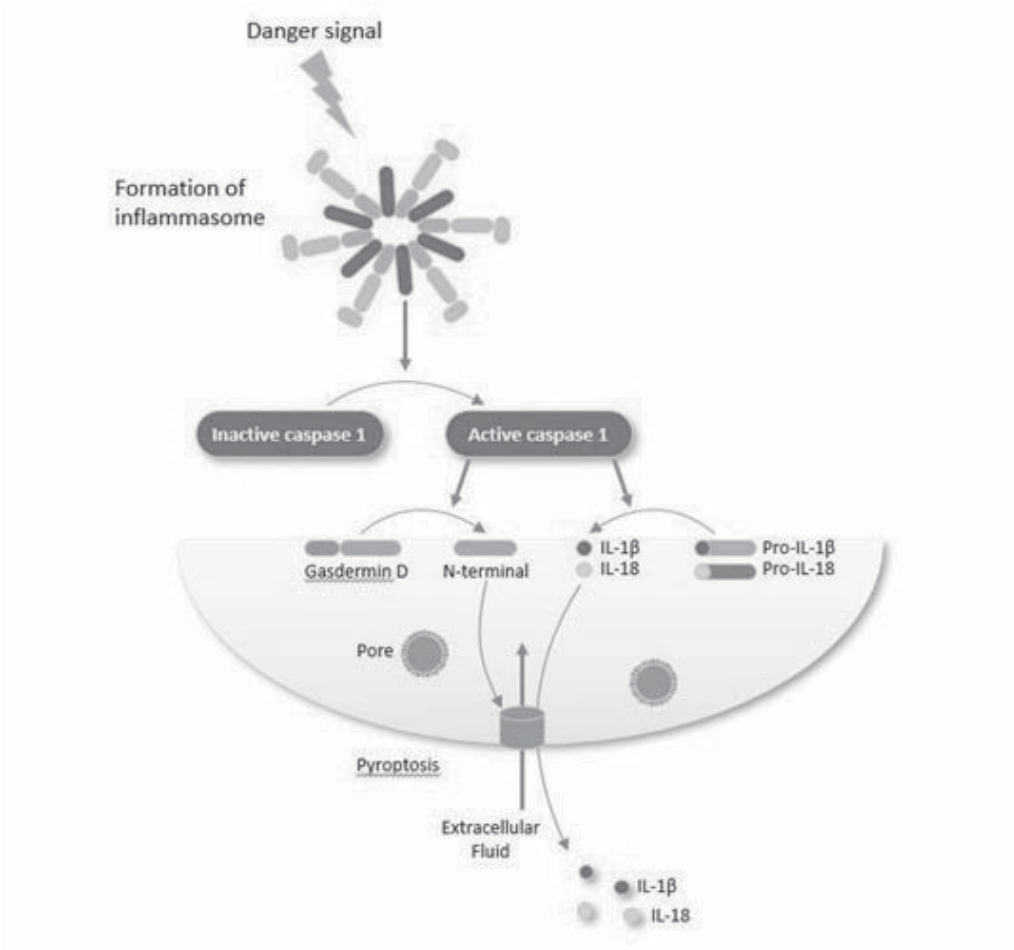


Background on Inflammasomes

Inflammasomes are multi-protein signaling complexes that control the inflammatory response and coordinate antimicrobial host defenses. They are activated by a range of pathogen-derived or environmental signals. Detection of these stimuli triggers formation of a large cytoplasmic multimolecular complex that serves to activate caspase 1. Upon activation, caspase 1 cleaves inactive pro-IL-1β into IL-1β. It also cleaves other IL-1 family cytokines, converting inert pro-IL-18 to active IL-18. Caspase 1 also can initiate a cell death

process, called pyroptosis, that rapidly releases inflammatory mediators, including, but not limited to, mature IL-1β and IL-18 (Figure 14). These inflammatory mediators recruit additional immune cells that are important to eradicate the infection or cellular injury. However, this feed forward loop, when dysregulated, also forms the basis of many auto-inflammatory diseases.

Figure 14: Role of inflammasomes



Rationale for Targeting NLRP3

NLRP3 is known to be activated by a range of non-infectious tissue damage signals associated with injury, aging, physical inactivity and obesity. When activated, NLRP3 initiates immune responses and stimulates production of inflammatory cytokines IL-1β and IL-18, as well as pyroptosis. Based on both animal model studies and clinical data, NLRP3 has been shown to be associated with a diverse range of diseases and conditions, including genetic NLRP3-dependent auto-inflammatory diseases (CAPS and related conditions), systemic diseases (cardiovascular, dermatologic and rheumatic conditions) and neuroinflammatory diseases (Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and multiple sclerosis), among others.

While the NLRP3 inflammasome historically has been a challenging drug target, the therapeutic potential of NLRP3 inhibitors in autoimmune disease has been validated by clinical and preclinical data and genetic evidence generated by third parties. Several clinical therapies targeting NLRP3-dependent cytokine anti-IL-1β have been approved, providing validation for its role in a broad range of inflammatory disorders. Approved therapies include Ilaris (canakinumab) for the treatment of Still's disease and multiple periodic fever syndromes, Kineret (anakinra) for the treatment of Neonatal onset multisystem inflammatory disease (NOMID) and Arcalyst (rilonacept) for the treatment of CAPS. However, the therapeutic window of these drugs is limited by an increased risk of serious infections.

An NLRP3 inhibitor may be less immunosuppressive and better tolerated than an anti-IL-1β therapy because (a) other pathogen-recognizing inflammasomes can be engaged to produce IL-1β, and (b) risk of infection may be lower as the effects of a small molecule therapy are easily reversible upon discontinuation of therapy (hours to days) compared to an antibody, which clears the body very slowly (days to weeks).

In addition, preclinical data has linked NLRP3 activation to over 20 diseases resulting from aberrant inflammation. The most widely used NLRP3 inhibitor reference molecule, MCC950, which has been the starting point for a number of drug discovery programs, suggests efficacy in a wide range of murine disease models that are NLRP3-dependent. Moreover, NLRP3 has been shown to be over-expressed and activated in tissues from patients suffering from a wide range of inflammatory diseases. Finally, gain-of-function mutations in the NLRP3 gene are associated with orphan inflammatory diseases, including CAPS, providing a genetic rationale for NLRP3 inhibition.

Our Solution: VTX2735

VTX2735 is an oral, selective small molecule inhibitor of NLRP3 that is peripherally restricted and designed for the treatment of systemic inflammatory diseases, such as cardiovascular, dermatologic and rheumatic diseases.

VTX2735 inhibits NLRP3 with an IC_{50} of approximately 80 nM in human whole blood as assessed via lipopolysaccharide (LPS)- and adenosine triphosphate (ATP)-induced IL-1β production. The *in vitro* potency of VTX2735 is greater than first-generation NLRP3 inhibitors, such as MCC950 (Table 2). VTX2735 demonstrated *in vitro* activity and dose-dependent reductions of IL-1β release in cells from patients with CAPS, a rare inflammatory autoimmune disease characterized by activating NLRP3 mutations.

Table 2: Comparison of *in vitro* potency of VTX2735 and MCC950 (Ventyx data)

IL-1ß IC_{50}	**VTX2735**	**MCC950**
Mouse Bone Marrow-Derived Macrophages	6 nM	18 nM
Human Monocytes	2 nM	9 nM
Human Whole Blood	80 nM	407 nM
CAPS Patient Monocytes	14-166 nM	>10,000 nM

Phase 1 Trial of VTX2735 in Healthy Volunteers

Overview

The Phase 1 SAD and MAD trial of VTX2735 was a two-part, randomized, double-blind, placebo controlled, dose-escalation study designed to evaluate the safety, tolerability and pharmacokinetics of single and multiple ascending doses. The study enrolled 72 adult healthy volunteers across SAD cohorts up to 200 mg and MAD cohorts up to 200 mg daily for 14 days.

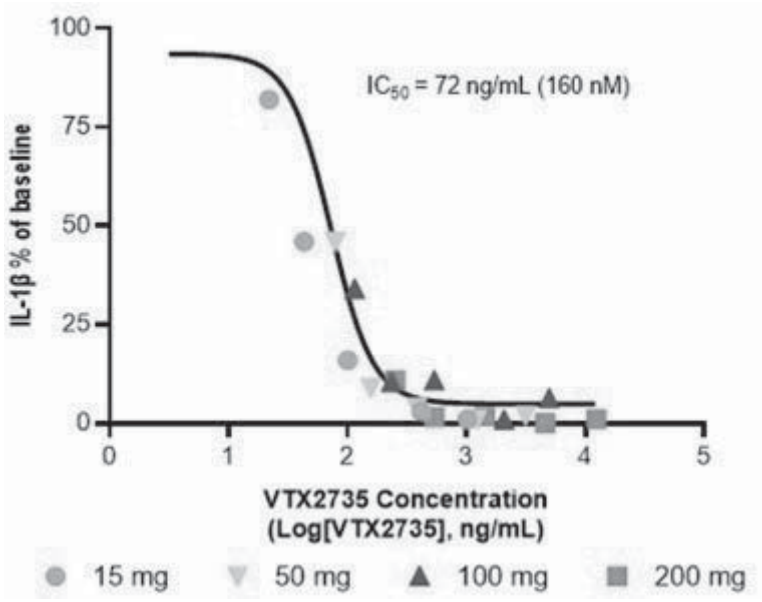
Safety and Tolerability

VTX2735 was well-tolerated across all dose cohorts and all subjects completed the trial. Drug exposures in both SAD and MAD cohorts increased linearly with dose. All drug-related AEs were considered mild, with no liver function test (LFT) abnormalities and no dose-related trend in the frequency of treatment-emergent AEs observed.

Pharmacodynamic Effects

Drug exposures also correlated with markers of target engagement as evidenced by strong PD activity in *ex vivo* LPS-plus ATP-mediated IL-1ß release assays from subject-derived plasma samples from both the SAD and MAD parts of the trial. VTX2735 demonstrated robust dose-related suppression of the induced pro-inflammatory cytokine IL-1ß release relative to placebo. VTX2735 also demonstrated reduction from baseline in high sensitivity C-reactive protein (hsCRP) concentrations.

Figure 15: Dose and Concentration-Dependent Suppression of IL-1ß *Ex Vivo*



Clinical Development Plan for VTX2735

Based on these positive Phase 1 results, we initiated a Phase 2 proof-of-concept trial for VTX2735 in CAPS patients in the first quarter of 2023. We expect to report topline data from the Phase 2 trial in the first quarter of 2024. We continue to evaluate additional indications for future clinical development of VTX2735.

CNS-Penetrant Inhibitor VTX3232

In addition to our peripheral NLRP3 inhibitor VTX2735 for systemic conditions, our portfolio of NLRP3 compounds includes VTX3232, a CNS-penetrant NLRP3 inhibitor with potential therapeutic utility for the treatment of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and MS, among others, based on preclinical and clinical evidence underscoring the pathogenic role of NLRP3 in these neurodegenerative diseases.

We optimized the activity of our lead series of CNS-penetrant compounds for NLRP3 inhibition in the various assays. In addition to in vitro activity in cellular assays, we profiled the compounds for CNS penetration by pharmacokinetic data in the mouse and in the rat. The brain and plasma concentrations in these studies were measured at various time points when dosed orally to determine the optimal pharmacokinetic profile for a CNS-penetrant NLRP3 inhibitor.

We are currently conducting a Phase 1 single and multiple ascending dose trial of VTX3232 in adult healthy volunteers. The trial is designed to assess the safety and tolerability of VTX3232 as well as target engagement and pharmacodynamic effect. The trial also includes dose cohorts with serial cerebrospinal fluid (CSF) sampling to assess drug exposure in the CSF. We expect to report topline results from the Phase 1 trial during the first quarter of 2024.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our scientific knowledge, technology and development experience provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any therapeutic candidates that we successfully develop and commercialize will compete with existing products and new products that may become available in the future.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage

companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize therapeutic 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 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.

The key competitive factors affecting the success of all of our therapeutic product candidates, if approved, are likely to be efficacy, safety, convenience, price, the level of competition, intellectual property protection and the availability of reimbursement from government and other third-party payors.

We expect to face competition from existing products and products in development for each of our product candidates.

Our success will be based in part on our ability to identify, develop and commercialize a portfolio of product candidates that have a lower risk of side effects and/or provide more symptomatic improvement than competing products.

In addition to specific competitors described below, there may be other early stage or pre-clinical programs that, if approved, would compete with our product candidates. Many of our competitors have substantially greater financial, technical and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

VTX002 and VTX958 (Inflammatory Bowel Disease)

VTX002, currently in development for the treatment of moderately to severely active UC, is an oral S1P1R modulator. VTX958, currently in development for the treatment of moderately to severely active CD, is an oral allosteric TYK2 inhibitor. If approved for the treatment of patients with moderately to severely active IBD, VTX002 and VTX958 would compete with: Zeposia (ozanimod), which is an S1P1R modulator marketed by BMS for UC; Velsipity (etrasimod), which is an S1P1R modulator marketed by Pfizer for UC; Entyvio (vedolizumab), which is an a4ß7 integrin antibody marketed by Takeda for UC and CD; Humira (adalimumab), which is a TNF antibody marketed by AbbVie Inc. for UC and CD; Stelara (ustekinumab), which is an IL-12/IL-23 antibody marketed by Johnson & Johnson for UC and CD; Omvoh (mirikizumab), which is an IL-23 antibody marketed by Eli Lilly for UC; Xeljanz (tofacitinib), which is a JAK1 inhibitor marketed by Pfizer Inc. for UC; Rinvoq (upadacitinib), which is a JAK1 inhibitor marketed by AbbVie for UC and CD; Jyseleca (filgotinib), which is a JAK1 inhibitor marketed in the European Union, Great Britain and Japan by Galapagos NV for UC; Simponi (golimumab), which is a TNF antibody marketed by Johnson & Johnson for UC; and Skyrizi (risankizumab), which is an anti-IL-23 antibody marketed by AbbVie, Inc. for CD.

We are aware of several companies with product candidates in development for the treatment of patients with moderately to severely active IBD, including: Roche's RVT-3101, an anti-TL1A antibody entering Phase 3; Merck's PRA023, an anti-TL1A antibody entering Phase 3; and risankizumab and guselkumab, which are anti-IL-23 antibodies being developed by AbbVie, Inc. and Janssen Pharmaceuticals N.V., respectively, in UC. We are also aware of additional product candidates in clinical development by AbbVie Inc., Abivax SA, Amgen Inc., Bausch Health Companies, Inc. (Salix Pharmaceuticals), BMS, Connect Biopharma Holdings Limited, Gilead Sciences, Inc., GlaxoSmithKline plc, Janssen Pharmaceuticals N.V., Landos Biopharma, Inc., Merck & Co., Inc., Morphic Therapeutic, Inc., Pfizer Inc., Protagonist Therapeutics, Inc., RedHill Biopharma Ltd. and Seres Therapeutics, Inc.

VTX2735 and VTX3232 (NLRP3 Inhibitor Portfolio)

VTX2735 is our lead peripherally restricted NLRP3 inhibitor, a class of medicines with no currently approved agents. We are also developing VTX3232 as our lead CNS-penetrant NLRP3 inhibitor candidate. We are aware of several other NLRP3 inhibitors in clinical development, including DFV890 from Novartis (Phase 2 trials ongoing); selnoflast (RG6418) from Roche AG (Phase 1); NT-0796 (Phase 2) and NT-0249 (Phase 1) from NodThera; VENT-01 (preclinical) and VENT-02 (Phase 1) from Ventus Therapeutics; and OLT-1177 (Phase 2) from Olatec Therapeutics LLC.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing. We intend to rely on third-party contract manufacturers for commercial manufacturing if our product candidates receive marketing approval. We believe there are multiple sources for all of the materials required for the manufacture of our product candidates. Our manufacturing strategy enables us to more efficiently direct financial resources to the research, development and commercialization of product candidates rather than diverting resources to develop manufacturing facilities internally. As our product candidates advance through development, we expect to enter into longer-term commercial supply agreements with key suppliers and manufacturers to fulfill and secure our production needs.

Intellectual Property

We strive to protect the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the U.S. and in jurisdictions outside of the U.S. directed to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position. We also plan to rely on data exclusivity, market exclusivity and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

VTX958

As of February 12, 2024, with respect to our TYK2 program, we own two U.S. patents, four pending U.S. patent applications, two international patent applications filed under the Patent Cooperation Treaty ("PCT"), and more than fifty pending foreign patent applications. More specifically, we own one U.S. patent, one pending U.S. patent application, and more than twenty pending foreign patent applications with claims directed to our lead product candidate VTX958, and other related compounds as a composition of matter, as well as claims directed to pharmaceutical compositions and uses of such compounds, including the use of VTX958, to treat inflammatory or autoimmune diseases, including Crohn's disease. Any patents that may issue from these pending applications directed to VTX958 are expected to expire in November 2040, absent any patent term adjustments or extensions. In addition, we own one pending U.S. patent application, one international patent application filed under the PCT, and two pending foreign patent applications (in Argentina and Taiwan) with claims directed to crystalline forms (polymorphs) of VTX958, as well as one international patent application filed under the PCT with claims directed to processes of making VTX958. Any patents that may issue from these additional pending applications directed to VTX958 are expected to expire between 2043 and 2044, absent any patent term adjustments or extensions.

VTX002

As of February 12, 2024, with respect to our S1P1R program, we own one U.S. patent, one pending U.S. patent application, more than forty foreign patents (including in various European countries, Australia, Brazil, China, Hong Kong, India, Israel, Japan, Macao, Mexico, and Russia), and seven pending foreign patent applications (in Canada, China, Europe, Hong Kong, Japan, Korea, and the Philippines) with claims directed to our lead product candidate VTX002, and other related compounds as a composition of matter, as well as claims directed to pharmaceutical compositions and uses of such compounds, including the use of VTX002, to treat UC. The issued patents, and any patents that may issue from these pending applications directed to VTX002, are expected to expire in November 2036 absent any patent term adjustments or extensions. In addition, we own one pending U.S. patent application, one international patent application filed under the PCT, and one pending foreign patent application (in Taiwan) with claims directed to crystalline forms (polymorphs) of VTX002, as well as one international patent application filed under the PCT with claims directed to processes of making VTX002. Any patents that may issue from these additional pending applications directed to VTX002 are expected to expire between 2043 and 2044, absent any patent term adjustments or extensions.

VTX2735 and VTX3232

As of February 12, 2024, with respect to our NLRP3 program, we own one U.S. patent, five pending U.S. patent applications, one pending U.S. provisional patent application, one international patent application filed under the PCT, and more than fifty pending foreign patent applications. More specifically, we own one U.S. patent, one pending U.S. patent application, and more than twenty pending foreign patent applications with claims directed to our lead product candidate VTX2735, and other related compounds as a composition

of matter, as well as claims directed to pharmaceutical compositions and uses of such compounds, including VTX2735. Any patents that may issue from these pending applications are expected to expire in March 2041, absent any patent term adjustments or extensions. Further, we own one pending U.S. patent application, one international patent application filed under the PCT, and two pending foreign patent applications (in Taiwan and Argentina) with claims directed to our lead product candidate VTX3232, and other related compounds as a composition of matter, as well as claims directed to pharmaceutical compositions and uses of such compounds, including VTX3232. Any patents that may issue from these pending applications directed to VTX3232 are expected to expire in March 2043, absent any patent term adjustments or extensions.

We also possess know-how and trade secrets relating to the development and commercialization of our product candidates.

With respect to our product candidates and processes we intend to develop and commercialize in the normal course of business, we intend to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. We may also pursue patent protection with respect to manufacturing and drug development processes and technologies.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the U.S. can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued U.S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the U.S. varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of immunology has emerged in the U.S. The relevant patent laws and their interpretation outside of the U.S. is also uncertain. Changes in either the patent laws or their interpretation in the U.S. and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and our issued patents may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

Government Regulation

Government authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the new drug application, or NDA, process before it may be legally marketed in the U.S.

U.S. Drug Development Process

In the U.S., the FDA regulates drugs, including small molecules, under the federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with Good Laboratory Practice, or GLP, regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, regulations to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to accept the filing for review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current GMP, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of other studies required by the FDA, including immunogenicity, carcinogenicity, genotoxicity and stability studies;
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the U.S.; and
- compliance with any post-approval requirements, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and the potential requirement to conduct post-approval studies.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An investigational new drug, or IND, sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. They must be conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject

selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND as well as any subsequent protocol amendments, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations.

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

- *Phase 1*: The product candidate is initially introduced into healthy human volunteers and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Sponsors sometimes designate their Phase 1 clinical trials as Phase 1a or Phase 1b. Phase 1b clinical trials are typically aimed at confirming dosing, pharmacokinetics and safety in larger number of patients. Some Phase 1b studies evaluate biomarkers or surrogate markers that may be associated with efficacy in patients with specific types of diseases.

- *Phase 2*: This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and appropriate dosage.

- *Phase 3*: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, generally at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

NDA Review and Approval Process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

The FDA may refer an application for a novel drug to an advisory committee. 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. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support

dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Unique to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious disease or condition. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. The Food and Drug Omnibus Reform Act made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements.

A sponsor may seek FDA designation of a product candidate as a "breakthrough therapy" if the product is intended, 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. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. The designation includes all of the fast track program features, which means that the sponsor may file sections of the NDA for review on a rolling basis if certain conditions are satisfied, including an agreement with FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. The breakthrough therapy designation is a

distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate. Depending on other factors that impact clinical trial timelines and development, such as our ability to identify and onboard clinical sites and rates of study participant enrollment and drop-out, we may not realize all the benefits of these expedited or accelerated review programs.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. In addition, the FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Any drug products manufactured or distributed by us or our partners pursuant to FDA approvals will be subject to pervasive and continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds on post-approval clinical trials, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

NDA Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year

exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the U.S. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity may offer a seven-year period of marketing exclusivity, except in certain circumstances.

In *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in *Catalyst*, FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst* order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

U.S. Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate for which we may seek regulatory approval. Sales in the U.S. will depend, in part, on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for our product candidates can be subject to challenge, reduction or denial by third-party payors.

The process for determining whether a third-party payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. A third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Additionally, in the U.S. there is no uniform policy among payors for coverage or reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. If coverage and adequate reimbursement are not available, or are available only at limited levels, successful commercialization of, and obtaining a satisfactory financial return on, any product we develop may not be possible.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for marketing, we may need to conduct expensive studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider our product candidates to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development.

U.S. Healthcare Reform

In the U.S., there has been, and continues 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 the profitable sale of product candidates.

Among policy makers and payors in the U.S., 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 U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, 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 ACA, among other things: (1) increased the minimum Medicaid rebates owed by manufacturers under the

Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; (2) created a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected; (3) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in certain government healthcare programs; (4) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (5) expanded the eligibility criteria for Medicaid programs; (6) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; (7) created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts 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; (8) established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (9) established a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, in June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and healthcare measures promulgated by the Biden administration will impact the ACA, our business, financial condition and results of operations. Complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and will remain in effect through 2032, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state 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 drug products. The American Rescue Plan Act of 2021 eliminated the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In August 2022, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. In an effort to curb Medicare Patients' out-of-pocket costs for prescription drugs, the Part D redesign legislation requires manufacturers to contribute to the catastrophic coverage phase for Part D drugs, as discounts through a manufacturer discount program. Furthermore, any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. Various industry stakeholders, including certain pharmaceutical companies and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. The impact of these judicial challenges, legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. Any reduction in reimbursement from Medicare or other government programs may result in a reduction in payments from private payors. The impact of legislative, executive and administrative actions of the Biden administration on us and the pharmaceutical industry as a whole is unclear.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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. Further, FDA recently authorized the state of Florida to import certain prescription drugs from Canada for a period of two years to help reduce drug costs, provided that Florida's Agency for Health Care Administration meets the requirements set forth by the FDA. Other states may follow Florida. We are unable to predict the future course of federal or state healthcare legislation in the U.S. directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Further, it is possible that additional governmental action will be taken in response to future public health emergencies, such as the COVID-19 pandemic. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our products candidates may lose regulatory approval that may have been obtained and we may not achieve or sustain profitability.

U.S. Healthcare Fraud and Abuse Laws and Compliance Requirements

Federal and state healthcare laws and regulations restrict business practices in the pharmaceutical industry. These laws include anti-kickback and false claims laws and regulations, data privacy and security and transparency laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. 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 civil False Claims Act and the Civil Monetary Penalties Statute.

The federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, prohibit, among other things, any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal civil and criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, imposes certain requirements relating to the privacy, security and transmission of protected health information on HIPAA covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates who conduct certain activities for or on their behalf involving protected health information on their behalf as well as their covered subcontractors.

The federal Physician Payments Sunshine Act requires applicable group purchasing organizations and applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to certain payments and other transfers of value made to covered recipients, including physicians licensed to practice in the U.S. (defined to include doctors of medicine and osteopathy, dentists, podiatrists, optometrists and licensed chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others) and teaching hospitals, in the previous year, as well as information regarding ownership and investment interests held by covered physicians and their immediate family members.

Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; 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, or otherwise restrict payments or transfers of value that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and

security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure compliance with applicable healthcare laws and regulations can involve substantial costs. Violations of healthcare laws can result in significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare programs, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of operations.

Foreign Regulation

In order to market any product outside of the U.S., we would need to 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 our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the U.S. apply similarly in the context of the European Union, or EU, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries or jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

To market a medicinal product in the European Economic Area, or EEA (which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein), we must obtain a Marketing Authorization, or MA. There are two types of marketing authorizations:

- the Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced therapy products and medicinal products containing a new active substance indicated for the treatment certain diseases, such as AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Data and Marketing Exclusivity

In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the 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.

Pediatric Investigation Plan

In the EEA, marketing authorization applications for new medicinal products not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension.

Clinical Trials

Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCPs. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products. If the sponsor of the clinical trial is not established within the European Union, it must appoint an entity within the European Union to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization from the competent authority, and a positive opinion from an independent ethics committee. The application for a clinical trial authorization must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Clinical trials in the European Union were regulated under European Council Directive 2001/20/EC (Clinical Trials Directive) on the implementation of GCP in the conduct of clinical trials of medicinal products for human use. In April 2014, Regulation EU No 536/2014 (Clinical Trials Regulation) was adopted to replace the Clinical Trials Directive. The Clinical Trials Regulation entered into application on January 31, 2022, and is intended to simplify the rules for clinical trial authorization and standards of performance. For instance, there is a streamlined application procedure via a single-entry point, a European Union portal and database. The new clinical trial portal and database is maintained by the EMA in collaboration with the European Commission and the European Union Member States. The objectives of the new Regulation include consistent rules for conducting trials throughout the European Union, consistent data standards and adverse events listing, and consistent information on the authorization status. Additionally, information on the conduct and results of each clinical trial carried out in the European Union will be made publicly available. A clinical trial may only be commenced after an Ethics Committee has given its approval. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP. Other national and European Union-wide regulatory requirements also apply.

Privacy and Data Protection Laws

We are subject to laws and regulations in non-U.S. countries covering data privacy and the protection of health-related and other personal information. EU member states and other jurisdictions have adopted data protection laws and regulations that impose significant compliance obligations. Laws and regulations in these jurisdictions apply broadly to the collection, use, storage, disclosure, processing and security of personal information that identifies or may be used to identify an individual, such as names, contact information, and sensitive personal data such as health data. These laws and regulations are subject to frequent revisions and differing interpretations, and have generally become more stringent over time.

In the European Union, or EU, the General Data Protection Regulation, or GDPR, imposes many requirements for controllers and processors of personal data, including, for example, high standards for obtaining consent from individuals to process their personal data, robust disclosures to individuals and a robust individual data rights regime, abbreviated timelines for data breach notifications, limitations on retention and secondary use of information, requirements pertaining to health data and pseudonymized (i.e., key-coded) data and obligations when we contract third-party processors in connection with the processing of the personal data. The GDPR allows EU member states to make additional laws and regulations further limiting the Processing of genetic, biometric or health data. Failure to comply with the requirements of GDPR and the applicable national data protection laws of the EU member states could subject us to regulatory sanctions, delays in clinical trials, criminal prosecution and/or civil fines or penalties. Changes to the GDPR and applicable

national laws related to privacy, data protection, and data security, including with respect to how these laws should be applied in the context of clinical trials or other transactions from which we may gain access to personal data, could increase our compliance costs and exposure to potential liability.

Employees and Human Capital Resources

As of December 31, 2023, we had 79 full-time employees and 1 part-time employee, 19 of whom have a Ph.D. or M.D. and 17 of whom were engaged in research and development activities. On December 5, 2023, we committed to and implemented a reduction in force that impacted approximately 20% of the Company's workforce. 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 resource objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Additional Information

We were incorporated in Delaware in November 2018. Our principal executive offices are located at 12790 El Camino Real, Suite 200 San Diego, CA 92130. Our telephone number is (760) 593-4832. Our website address is https://ventyxbio.com/. We make available on our website, free of charge, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to those reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or SEC. Our SEC reports can be accessed through the investor relations page of our website located at https://ir.ventyxbio.com/. The SEC also maintains a website that contains our SEC filings. The address of the site is www.sec.gov.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as all other information included in this Annual Report. If any of the following risks actually occurs, our business, financial condition, results of operations, prospects and ability to accomplish our strategic objectives could be materially harmed. As a result, the market 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 deem immaterial may also impair our business operations and the market price of our common stock.

Risk Factors Summary

Our business is subject to numerous risks and uncertainties, including those outside of our control that could cause our actual results to be harmed, including risks regarding the following:

- We have a history of operating losses and have incurred significant losses since our inception. We expect to continue to incur significant losses and we may never be profitable;
- We will need to obtain substantial additional financing for the development and any commercialization of our product candidates, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development efforts or other operations;
- Our limited operating history, and the biotechnology industry in which we operate, make it difficult to evaluate our business plan and our prospects;
- Our business depends entirely on the success of our product candidates and we cannot guarantee that these product candidates will successfully complete development, receive regulatory approval, or be successfully commercialized. If we are unable to develop, receive regulatory approval for, and ultimately successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed;
- Our clinical trials may fail to demonstrate adequately the safety and efficacy of our product candidates, which would prevent or delay regulatory approval and commercialization;

- Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of early, smaller-scale studies and clinical trials with a single or few clinical trial sites may not be predictive of eventual safety or effectiveness in large-scale pivotal clinical trials across multiple clinical trial sites. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all;

- We face significant competition from other biotechnology and pharmaceutical companies;

- We may use our limited financial and human resources to pursue a particular type of treatment, or treatment for a particular type of disease, and fail to capitalize on programs or treatments of other types of diseases that may be more profitable or for which there is a greater likelihood of success;

- We may develop product candidates in combination with other therapies, which exposes us to additional risks and could result in our products, even if approved, being removed from the market or being less successful commercially;

- It may take longer and cost more to complete our clinical trials than we project, or we may not be able to complete them at all;

- The FDA regulatory approval process is lengthy, time-consuming and unpredictable, and we may experience significant delays in the clinical development and regulatory approval of our product candidates;

- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, we may not be able to compete effectively or operate profitably; and

- Our stock price has been and may continue to be volatile and could fluctuate widely in response to many factors, including, without limitation, announcements of the results of clinical trials by us, our collaborators or our competitors, or positive or negative developments with respect to similar products, including those being developed by our collaborators or our competitors.

Risks Related to Our Business

We have a history of operating losses and have incurred significant losses since our inception. We expect to continue to incur significant losses and we may never be profitable.

Since our inception in November 2018, we have incurred significant operating losses, we have not generated any revenue from operations to date and, through the date of this report, have financed our operations primarily through public offerings and private placements of our common stock, private placements of our convertible preferred stock and convertible debt instruments. We do not have any products approved for commercial sale or for which marketing approval has been sought. During the year ended December 31, 2023, we incurred a net loss of $193.0 million, compared with a net loss of $108.4 million for the year ended December 31, 2022. As of December 31, 2023, we had an accumulated deficit of $419.2 million. We do not expect to generate any meaningful revenue from product sales, unless and until we successfully complete development and obtain marketing approval for one or more of our product candidates, which we do not expect to happen for at least the next several years, if ever. We expect to incur significant and increasing operating losses in the future. The operating losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

Our ability to achieve profitability in the future is dependent upon obtaining regulatory approvals for our products and successfully commercializing our products alone or with third parties. However, our operations may not be profitable even if one or more of our product candidates under development are successfully developed, approved and thereafter commercialized.

We will need to obtain substantial additional financing for the development and any commercialization of our product candidates, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development efforts or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations and expect our expenses may increase substantially in the foreseeable future. As of December 31, 2023, we had an accumulated deficit of $419.2 million. Developing our product candidates and conducting clinical trials requires substantial amounts of capital. Our research and development and our operating costs have also

been substantial and are expected to increase. We will also require a significant additional amount of capital to commercialize any approved products.

As of December 31, 2023, we had cash, cash equivalents and marketable securities of $252.2 million, excluding restricted cash of $1.0 million. In September 2021, we raised gross proceeds of $51.0 million in cash in connection with the sale of our Series B Convertible Preferred Stock. In October 2021, we raised gross proceeds of $174.3 million in connection with the sale of common stock in our initial public offering. In September 2022, we raised gross proceeds of $176.6 million in connection with the sale of common stock in a private placement to certain qualified institutional buyers and institutional accredited investors. In February 2023, we raised gross proceeds of $50.0 million in connection with the sale of common stock through our Open Market Sales Agreement℠ (Sales Agreement) with Jefferies LLC (Jefferies), as sales agent. We are using and expect to continue to use our existing cash, cash equivalents and marketable securities to fund expenses in connection with our ongoing and any future clinical trials, our third-party manufacturing costs and the hiring of additional personnel, and for other research and development activities, working capital and general corporate purposes. We believe that existing cash, cash equivalents, and marketable securities will be sufficient to fund our obligations for at least twelve months from the issuance of this Annual Report on Form 10-K. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to be available to fund our operations is based on assumptions that may be proved inaccurate, and we could deplete our available capital resources sooner than we currently expect. We will require additional capital for the further development and any commercialization of our product candidates and will need to raise additional funds sooner than we anticipate if we choose to expand more rapidly.

Our future capital requirements may depend on, and could increase significantly as a result of, many factors, including:

- the timing of, and the costs involved in, preclinical and clinical development and obtaining any regulatory approvals for our product candidates;
- the costs of manufacturing and distributing our product candidates and any products for which we receive regulatory approval, if any;
- any other product candidates we develop or acquire;
- our ability to establish and maintain strategic partnerships, licensing or other commercialization arrangements and the terms and timing of such arrangements;
- the degree and rate of market acceptance of any approved products;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing intellectual property claims, including litigation costs and the outcome of such litigation;
- the costs related to commercializing product candidates independently;
- the timing, receipt and amount of sales of, or royalties on, any approved products; and
- any product liability or other lawsuits related to our product candidates or the company.

Any 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 may develop in the future, if approved. Adequate additional financing may not be available to us in sufficient amounts or on acceptable terms, or at all. 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 may include liquidation or other preferences that adversely affect your rights as a stockholder and the possibility of such issuance may cause the market price of our shares to decline. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect the conduct of our business. If we raise additional funds through up-front payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to certain of our technologies or our product candidates, or

grant licenses on terms that are not favorable to us, which may have a material adverse effect on our business, operating results and prospects. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the COVID-19 pandemic, the conflicts in Eastern Europe and the Middle East, and otherwise. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to significantly delay, reduce the scope of, suspend or eliminate one or more of our research or development programs, clinical trials or future commercialization efforts.

Our limited operating history, and the biotechnology industry in which we operate, make it difficult to evaluate our business plan and our prospects.

We are an early-stage company and were founded in November 2018 and have a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have only a limited operating history on which a decision to invest in our company can be based and against which we can test the plans and assumptions in our business plan, and investors therefore may have difficulty evaluating the likelihood of our success. The future of our company is dependent upon our ability to implement our business plan, as that business plan may be modified from time to time by our management and board of directors.

We face the problems, expenses, difficulties, complications and delays normally associated with a pre-commercial biotechnology company, many of which are beyond our control. Accordingly, our prospects should be considered in light of the risks, expenses and difficulties frequently encountered in the establishment of a new business developing product candidates in an industry that is characterized by a number of market entrants and intense competition. Because of our size and limited resources, we may not possess the ability to successfully overcome many of the risks and uncertainties frequently encountered by pre-commercial companies involved in the rapidly evolving field of immunology. If we do not address these risks successfully, our business will suffer. In addition, as a new business, we may encounter other unforeseen expenses, difficulties, complications, delays, and other known and unknown factors. Even if our research and development efforts are successful, we may also face the risks associated with the transition from development to commercialization of new products. We may not be successful in such a transition. There can be no assurance that we will be successful in developing our business. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

Our business depends entirely on the success of our product candidates and we cannot guarantee that these product candidates will successfully complete development, receive regulatory approval, or be successfully commercialized. If we are unable to develop, receive regulatory approval for, and ultimately successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We currently have no products approved for commercial sale or for which regulatory approval to market has been sought. We have invested a significant portion of our efforts and financial resources in the development of our lead product candidates targeting S1P1R, TYK2 and NLRP3, each of which is in clinical development, and expect that we will continue to invest heavily in these product candidates, as well as in any future product candidates we may develop. Our business depends entirely on the successful development, regulatory approval and commercialization of our product candidates, each of which may never occur. Our ability to generate revenues, which we do not expect will occur for many years, if ever, is substantially dependent on our ability to develop, obtain regulatory approval for, and then successfully commercialize our product candidates, which may never occur.

Our product candidates will require substantial additional clinical and non-clinical development time, regulatory approval, commercial manufacturing arrangements, establishment of a commercial organization, significant marketing efforts, and further investment before we can generate any revenue from product sales. We currently generate no revenue and we may never be able to develop or commercialize any products. We cannot assure you that we will meet our timelines for our current or future clinical trials, which may be delayed or not completed for a number of reasons. Our product candidates are susceptible to the risks of failure inherent at any stage of product development, including the appearance of unexpected adverse events, failure to achieve primary endpoints in clinical trials or failure to meet certain internal targets to support further development. For example, in the fourth quarter of 2023, we announced topline data from a Phase 2 trial of VTX958 in moderate to severe plaque psoriasis. While the study achieved its primary and key secondary endpoints, the efficacy results did not meet our internal target to support further development of VTX958 in psoriasis. Based on these results, we have elected to terminate ongoing activities in the Phase 2 trials of VTX958 in plaque psoriasis and psoriatic arthritis.

Even if our product candidates are successful in clinical trials, we are not permitted to market or promote any of our product candidates before we receive regulatory approval from the U.S. Food and Drug Administration, or the FDA, or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates or regulatory approval that will allow us to successfully commercialize our product candidates. If we do not receive FDA or comparable foreign regulatory approval with the necessary conditions to allow commercialization, we will not be able to generate revenue from those product candidates in the United States or elsewhere in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing our product candidates will have a material adverse impact on our business and financial condition.

We have not previously submitted a New Drug Application, or NDA, for any small molecule product candidates or similar marketing application to the FDA or comparable foreign regulatory authorities, for any product candidate, and we cannot be certain that our current or any future product candidates will be successful in clinical trials or receive regulatory approval. Furthermore, although we do not expect to submit an NDA with comparisons to existing or more established therapies and we do not expect the FDA to base its determination with respect to product approval on such comparisons, the FDA may factor these comparisons into its decision whether to approve our product candidates. The FDA may also consider its approvals of competing products, which may alter the treatment landscape concurrently with their review of our NDA filings, and which may lead to changes in the FDA's review requirements that have been previously communicated to us and our interpretation thereof, including changes to requirements for clinical data or clinical study design. Such changes could delay approval or necessitate withdrawal of our NDA filings.

If approved for marketing by applicable regulatory authorities, our ability to generate revenues from our product candidates will depend on our ability to:

- price our product candidates competitively such that third-party and government reimbursement leads to broad product adoption;
- prepare a broad network of clinical sites for administration of our product;
- create market demand for our product candidates through our own marketing and sales activities, and any other arrangements to promote these product candidates that we may otherwise establish;
- receive regulatory approval for the targeted patient population(s) and claims that are necessary or desirable for successful marketing;
- effectively commercialize any of our product candidates that receive regulatory approval;
- manufacture product candidates through contract manufacturing organizations, or CMOs, or in our own, or our affiliates', manufacturing facility in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter;
- establish and maintain agreements with wholesalers, distributors, pharmacies, and group purchasing organizations on commercially reasonable terms;
- obtain, maintain, protect and enforce patent and other intellectual property protection and regulatory exclusivity for our product candidates;
- maintain compliance with applicable laws, regulations, and guidance specific to commercialization including interactions with health care professionals, patient advocacy groups, and communication of health care economic information to payors and formularies;
- achieve market acceptance of our product candidates by patients, the medical community, and third-party payors;
- achieve appropriate reimbursement for our product candidates;
- maintain a distribution and logistics network capable of product storage within our specifications and regulatory guidelines, and further capable of timely product delivery to commercial clinical sites;
- effectively compete with other therapies or competitors; and
- assure that our product candidates will be used as directed and that additional unexpected safety risks will not arise.

It may take longer and cost more to complete our clinical trials than we project, or we may not be able to complete them at all.

For budgeting and planning purposes, we have projected the date for the commencement of future trials, and continuation and completion of our ongoing clinical trials. However, a number of factors, including scheduling conflicts with participating clinicians and clinical institutions, and difficulties in identifying and enrolling patients who meet trial eligibility criteria, may cause significant delays. We may not commence or complete clinical trials involving any of our products as projected or may not conduct them successfully.

Our ability to enroll or treat patients in our clinical trials, or the duration or costs of those clinical trials, could be affected by multiple factors, including, preliminary clinical results, which may include efficacy and safety results, but may not be reflected in the final analyses of these clinical trials. Depending on the outcome of our clinical trials, we may need to conduct one or more follow-up or supporting clinical trials in order to develop our products for FDA approval. Many companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in late-stage clinical trials even after achieving positive results in earlier development, and we cannot be certain that we will not face such setbacks.

Furthermore, the timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Accordingly, we cannot guarantee that the trial will progress as planned or as scheduled. Delays in enrollment may result in increased costs or may affect the timing or outcome of our ongoing clinical trial and planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

Our clinical trials may fail to demonstrate adequately the safety and efficacy of our product candidates, which would prevent or delay regulatory approval and commercialization.

The clinical trials of our product candidates are, and, if approved, the manufacturing and marketing of our products will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. For our small molecule product candidates, we will need to demonstrate that they are safe and effective for their target indications and must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. Regulatory authorities may ultimately disagree with our chosen endpoints or may find that our clinical studies or clinical study results do not support product approval. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. For example, in the fourth quarter of 2023, we announced topline data from a Phase 2 trial of VTX958 in moderate to severe plaque psoriasis. While the study achieved its primary and key secondary endpoints, the efficacy results did not meet our internal target to support further development of VTX958 in psoriasis. Based on these results, we have elected to terminate ongoing activities in the Phase 2 trials of VTX958 in plaque psoriasis and psoriatic arthritis.

There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. Preclinical studies may also reveal unfavorable product candidate characteristics, including safety concerns. Many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization. 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 clinical trial protocols and the rate of dropout among clinical trial participants. Our current and future clinical trial results may not be successful. Moreover, should there be a flaw in a clinical trial or cross-site variation that are not properly addressed, it may not become apparent until the clinical trial is well advanced or until data from different sites become available. For example, our clinical trials are conducted at multiple sites in different geographies, with different levels of experience and expertise by medical professionals, and these professionals may make mistakes or introduce site-specific variation that could have an impact on the clinical data or on clinical trials by disqualifying patients or impacting patient ability to continue in a study.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of early, smaller-scale studies and clinical trials with a single or few clinical trial sites may not be predictive of eventual safety or effectiveness in large-scale pivotal clinical trials across multiple clinical trial sites. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive nonclinical studies and clinical trials that our product candidates are both safe and effective for each target indication. Preclinical and clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical study and clinical trial processes, and, because our product candidates are in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Although product candidates may demonstrate promising results in preclinical studies and early clinical trials, they may not prove to be safe or effective in subsequent clinical trials. For example, testing on animals occurs under different conditions than testing in humans and therefore, the results of animal studies may not accurately predict safety and effectiveness in humans. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials.

Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. Likewise, early, smaller-scale studies and clinical trials with a single or few clinical trial sites may not be predictive of eventual safety or effectiveness in large-scale pivotal clinical trials across multiple clinical trial sites. Even if data from a pivotal clinical trial are positive, regulators may not agree that such data are sufficient for approval and may require that we conduct additional clinical trials, which could materially delay our anticipated development timelines, require additional funding for such additional clinical trials, and adversely impact our business. Most product candidates that commence preclinical studies and clinical trials are never approved as products.

In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Drug-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, some of the clinical trials we conduct in the future may be open-label in study design and may be conducted at a limited number of clinical sites on a limited number of patients. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the institutional review boards, or IRBs, of the institutions in which such clinical trials are being conducted, by a data safety monitoring board for such clinical trial or by the FDA or comparable foreign regulatory authorities. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the trial design or implementation of our clinical trials;
- changes in governmental regulations, including FDA policies and regulatory requirements for clinical trials and standards or data requirements for pharmaceutical approval or administrative actions;
- delays in our ability to commence a clinical trial;

- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining IRB approval at each clinical trial site;
- recruiting an adequate number of suitable patients to participate in a clinical trial;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- having subjects complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial;
- failure to demonstrate a clinical benefit from using a product candidate;
- addressing subject safety concerns that arise during the course of a clinical trial;
- adding a sufficient number of clinical trial sites; or
- obtaining sufficient product supply of product candidate for use in preclinical studies or clinical trials from third-party suppliers.

Further, conducting clinical trials in foreign countries can present additional risks that may delay completion of our clinical trials, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- diminished protection of intellectual property in some countries;
- the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of cultural differences in medical practices and clinical research;
- managing additional administrative burdens associated with foreign regulatory schemes; and
- interruptions or delays in our clinical trials resulting from geopolitical events, such as war or terrorism.

In particular, we are currently conducting a Phase 2 trial of VTX002 in patients with moderate-to-severe ulcerative colitis (UC). Enrollment has completed in the Phase 2 trial of VTX002 in ulcerative colitis and we reported positive results from the trial in the fourth quarter of 2023. The long-term extension period of the trial remains ongoing. While enrollment in this trial has concluded, our operations at additional sites in the region could also be impacted in future clinical trials of VTX002. The ongoing conflict has also impacted site selection in the ongoing Phase 2 trial of VTX958 in moderate-to-severe Crohn's disease, for which enrollment is ongoing. Additionally, if our relationships with any of our CROs is terminated, we may be unable to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. Furthermore, the United States and its European allies have imposed significant new sanctions against Russia and Belarus, including regional embargoes, full blocking sanctions, and other restrictions targeting major Russian financial institutions. Our ability to conduct clinical trials in Russia, Belarus, Ukraine and elsewhere in the region may also become restricted under applicable sanctions laws.

Moreover, 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 or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical 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 or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

If the results of our current and future clinical trials are inconclusive with respect to the efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may:

- incur unplanned costs;
- be delayed in or prevented from obtaining marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings including boxed warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities and receipt of necessary marketing approvals could be delayed or otherwise adversely affected.

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

- the size and nature of the patient population;
- the number of ongoing and planned clinical trials in the indications that we are pursuing, such as UC and Crohn's disease (CD), which have very slow enrollment rates;
- the severity of the disease under investigation;
- the patient eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary or secondary endpoints;
- the proximity of patients to trial sites;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials and the effectiveness of recruiting publicity;

- the patient referral practices of physicians;
- physicians' willingness to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our clinical trials;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate or enrollment in these clinical trials may be slower than we anticipate, potentially affecting our timelines for approval of our product candidates;
- patients that enroll in our clinical trials may misrepresent their eligibility or may otherwise not comply with the clinical trial protocol, resulting in the need to drop such patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- clinical investigators enrolling patients who do not meet the enrollment criteria, requiring the inclusion of additional patients in the clinical trial;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating;
- approval of new indications for existing therapies or approval of new therapies in general;
- our contracted clinical sites' or investigators' ability to obtain and maintain patient consents;
- amendments to our clinical protocols, which may affect enrollment in, or results of, our clinical trials, including amendments we have made to further define the patient population to be studied;
- the impact of material adverse events, such as the COVID-19 pandemic, which may affect the conduct of a clinical trial, including by slowing potential enrollment or reducing the number of eligible patients for clinical trials; and
- the risk that patients enrolled in clinical trials will not complete a clinical trial, return for post-treatment follow-up, or follow the required study procedures. For instance, patients, including patients in any control groups, may withdraw from the clinical trial if they are not experiencing improvement in their underlying disease or condition. Withdrawal of patients from our clinical trials may compromise the quality of our data.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators is limited, we may need to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our product candidates represent a departure from more commonly used treatments for inflammatory diseases and autoimmune disorders, potential patients and their doctors may be inclined to use conventional therapies rather than enroll patients in any future clinical trial. Additionally, patients, including patients in any control groups, may withdraw from the clinical trial if they are not experiencing improvement in their underlying disease or condition. Withdrawal of patients from our clinical trials may compromise the quality of our data.

Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment or small population size may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these clinical trials and adversely affect our ability to advance the development of our product candidates.

Interim, initial, "top-line" and preliminary 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 preliminary or top-line data from our preclinical studies and clinical trials, which are based on preliminary analyses 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 preclinical study or clinical 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 top-line or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and 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 or as patients from our clinical trials continue other treatments for their disease. Adverse differences between 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 could have a material adverse effect on the success of our business. 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 material or otherwise appropriate information to include in our disclosure. If the interim, top-line 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, results of operations, prospects or financial condition. Further, disclosure of interim, top-line or preliminary data by us or by our competitors could result in volatility in the price of our common stock.

We face significant competition from other biotechnology and pharmaceutical companies.

Competition in the treatment of inflammatory diseases and autoimmune disorders is intense and is accentuated by the rapid pace of technological development. Research and discoveries by others may result in breakthroughs which may render our product candidates obsolete even before they are approved or generate any revenue. There are products that are approved and currently under development by others that could compete with the product candidates that we are developing. Our competitors may:

- develop safer, more convenient or more effective therapeutic products;
- develop therapeutic products that are less expensive or have better reimbursement from private or public payors;
- reach the market more rapidly, reducing the potential sales of our products; or
- establish superior proprietary positions.

Due to the promising clinical therapeutic effect of competitor therapies in clinical trials, we anticipate substantial direct competition from other organizations developing treatments for inflammatory diseases and autoimmune disorders, such as UC and CD. In particular, we expect to compete with other new therapies for our lead indications developed by companies such as Bristol-Myers Squibb (BMS), Pfizer and others. Many of these companies and our other current and potential competitors have substantially greater research and development capabilities and financial, scientific, regulatory, manufacturing, marketing, sales, human resources and experience than we do. Many of our competitors have several therapeutic products that have already been developed, approved and successfully commercialized, or are in the process of obtaining regulatory approval for their therapeutic products in the United States and internationally. Our competitors may obtain regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in competitors establishing a strong market position before we are able to enter the market.

Universities and public and private research institutions in the United States and Europe are also potential competitors. While these universities and public and private research institutions primarily have educational objectives, they may develop proprietary technologies that lead to other FDA approved therapies or that secure patent protection that we may need for the development of our product candidates and that can be licensed or sold to other parties, including our competitors.

We are developing our lead product candidates, VTX958, VTX002, VTX2735 and VTX3232, for the treatment of inflammatory diseases and autoimmune disorders, including moderately to severely active ulcerative colitis and Crohn's disease. Currently, there are numerous companies that are developing various alternate treatments for these indications. With respect to VTX958, if approved, it would compete with injected biologic therapies and non-injectable systemic therapies approved or in development for the treatment of Crohn's disease. With respect to VTX002, if approved, it would compete with a number of companies developing product candidates, as well as Zeposia (ozanimod), which is an S1P receptor modulator marketed by BMS, and Velsipity (etrasimod), which is an S1P receptor modulator marketed by Pfizer. With respect to VTX2735 and VTX3232, we are aware of several other NLRP3 inhibitors in clinical or preclinical

development, including Inzomelid and Somalix being developed by Roche. Accordingly, our lead product candidates will face significant competition from multiple companies. Even if we obtain regulatory approval for our lead product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our products. We may not be able to implement our business plan if the acceptance of our products is inhibited by price competition or the reluctance of physicians to switch from other methods of treatment to our product, or if physicians switch to other new therapies, drugs or biologic products or choose to reserve our product for use in limited circumstances.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents or other intellectual property relating to our competitors' products, and our competitors may allege that our product candidates infringe, misappropriate or otherwise violate their intellectual property. See "—Risks Related to Intellectual Property."

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. 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 and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We have limited experience as a company conducting clinical trials and have relied and will rely on third parties and related parties to conduct our preclinical studies and clinical trials. Any failure by a third party, related party, or by us to conduct the clinical trials according to Good Clinical Practice and Good Manufacturing Practice, and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We expect to rely on medical institutions, academic institutions or contract research organizations, or CROs, to conduct, supervise or monitor some or all aspects of clinical trials involving our product candidates. We will have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own. If we fail to commence or complete, or experience delays in, any of our planned clinical trials, our stock price and our ability to conduct our business as currently planned could be harmed.

We have a limited history of conducting clinical trials and have no experience as a company in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety or efficacy for that indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities and clinical trial sites by, applicable regulatory authorities.

Large-scale clinical trials require significant financial and management resources, and reliance on third-party clinical investigators, CROs, CMOs, partners or consultants. Relying on third-party clinical investigators, CROs or CMOs may force us to encounter delays and challenges that are outside of our control. We may not be able to demonstrate sufficient comparability between products manufactured at different facilities to allow for inclusion of the clinical results from patients treated with products from these different facilities, in our product registrations. Further, our CMOs may not be able to manufacture our product candidates or otherwise fulfill their obligations to us because of interruptions to their business, including the loss of their key staff or interruptions to their raw material supply.

Our reliance on these third parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable trial protocol and legal, regulatory and scientific standards, and our reliance on the CROs, clinical trial sites, and other third parties does not relieve us of these responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial and for ensuring that our preclinical studies are conducted in accordance with GCP, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with Good Clinical Practice, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections (including pre-approval inspections once an NDA is filed with the FDA) of trial sponsors, clinical investigators, trial sites and certain third parties including CMOs and CROs. If we, our CROs, clinical trial sites, or other third parties fail to comply with applicable GCP or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations.

Our clinical trials must be conducted with product candidates that were produced under current Good Manufacturing Practices, or cGMP, regulations. Our failure to comply or our CMOs' failure to comply with these cGMP regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so could result in enforcement actions and adverse publicity.

We also rely on third parties other than our CMOs to manufacture, package, label and ship our product candidates for the clinical trials that we conduct. We may also find that the manufacture of our product candidates is more difficult than anticipated, resulting in an inability to produce a sufficient amount of our product candidates for our clinical trials or, if approved, commercial supply. Moreover, because of the complexity and novelty of our manufacturing process, there are only a limited number of manufacturers who have the capability of producing our product candidates. Should any of our contract manufacturers no longer produce our product candidates, it may take us significant time to find a replacement, if we are able to find a replacement at all. Any performance failure on the part of these third parties could delay clinical development or marketing approval of our product candidates or commercialization of our product candidates, if approved, producing additional losses and depriving us of potential product revenue.

Our CMOs, CROs, clinical trial sites and other third parties may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other therapeutic development activities that could harm our competitive position. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with them, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical trials and preclinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical trial protocols, regulatory requirements or for other reasons, our clinical trials may need to be repeated, extended, delayed or terminated. In the event we need to repeat, extend, delay or terminate our clinical trials, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates, and we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates or we or they may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be materially and adversely affected.

If any of our relationships with these third parties terminate, we may not be able to enter into alternative arrangements or do so on commercially reasonable terms. Switching or adding additional contractors involves additional cost and time and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. In addition, if an agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely.

We announced positive results from the Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis during the fourth quarter of 2023. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024. Additionally, we are conducting a Phase 2 trial of our peripheral NLRP3 inhibitor VTX2735 in patients with Cryopyrin-Associated Periodic Syndrome (CAPS), and a Phase 1 trial of our novel CNS-penetrant NLRP3 inhibitor VTX3232 in adult healthy volunteers. Our relative lack of experience conducting clinical trials may contribute to our planned clinical trials not beginning or completing on time, if at all. Large-scale clinical trials will require significant additional resources and reliance on CROs, clinical investigators or consultants. Consequently, our reliance on outside parties may introduce delays beyond our control. Our CROs and other third parties must communicate and coordinate with one another in order for our trials to be successful. Additionally, our CROs and other third parties may also have relationships with other commercial entities, some of which may compete with us. If our CROs or other third parties conducting our clinical trials do not perform their contractual duties or regulatory obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical trial protocols, GCP or other regulatory requirements or for any other reason, we may need to conduct additional clinical trials or enter into new arrangements with alternative CROs, clinical investigators or other third parties. We may be unable to enter into arrangements with alternative CROs on commercially reasonable terms, or at all.

We and the third parties upon which we rely are required to comply with GCP. GCP are regulations and guidelines enforced by regulatory authorities around the world, through periodic inspections, for products in clinical development. If we or these third parties fail to comply

with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and have to be repeated, and our submission of marketing applications may be delayed or the regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We are subject to the risk that, upon inspection, a regulatory authority will determine that any of our clinical trials fails to comply or failed to comply with applicable GCP regulations. In addition, our clinical trials must be conducted with material produced under GMP regulations, which are enforced by regulatory authorities. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be significantly impacted if our CROs, clinical investigators or other third parties violate federal or state healthcare fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

We also anticipate that part of our strategy for pursuing the wide range of indications potentially addressed by our product candidates may involve further investigator-initiated clinical trials. While these trials generally provide us with valuable clinical data that can inform our future development strategy in a cost-efficient manner, we generally have less control over not only the conduct but also the design of these clinical trials. Third-party investigators may design clinical trials involving our product candidates with clinical endpoints that are more difficult to achieve or in other ways that increase the risk of negative clinical trial results compared to clinical trials we may design on our own. Negative results in investigator-initiated clinical trials, regardless of how the clinical trial was designed or conducted, could have a material adverse effect on our prospects and the perception of our product candidates.

Moreover, 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/or a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. 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 regulatory approval of one or more of our product candidates.

We may be required to conduct additional clinical trials or modify current or future clinical trials.

Clinical testing is expensive, time consuming and subject to uncertainty. We cannot guarantee that any current or future clinical studies will be conducted as planned or completed on schedule, if at all, or that any of our product candidates will receive regulatory approval. We are presently conducting trials in multiple indications, such as moderately to severely active ulcerative colitis and Crohn's disease, among others. Even as these trials progress, issues may arise that could require us to suspend or terminate such clinical trials or could cause the results of one cohort to differ from a prior cohort. For example, we may experience slower than anticipated enrollment in our clinical trials, which may consequently delay our NDA filing timelines or permit competitors to obtain approvals that may alter our NDA filing strategy. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the clinical trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional clinical trials in support of potential approval of our product candidates.

Events that may prevent successful or timely initiation or completion of clinical development include:

- regulators or Institutional Review Boards, or IRBs, may not authorize us or our investigators to commence a clinical trial, conduct a clinical trial at a prospective trial site, or amend trial protocols, or regulators or IRBs may require that we modify or amend our clinical trial protocols;
- delays in reaching a consensus or inability to obtain agreement with regulatory agencies on study design or eligibility criteria for patient enrollment;
- the FDA or comparable foreign regulatory authorities may disagree with our intended indications, study design or our interpretation of data from preclinical studies and clinical trials or find that a product candidate's benefits do not outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may not accept data from studies with clinical trial sites in foreign countries (e.g., Australia, Poland, Germany, Belgium, Georgia, Hungary, Israel and Italy);

- the FDA may not allow us to use the clinical trial data from a research institution to support an IND if we cannot demonstrate the comparability of our product candidates with the product candidate used by the relevant research institution in its clinical studies;
- delays in or failure to reach an agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;
- imposition of a temporary or permanent clinical hold, suspensions or terminations by regulatory agencies, IRBs, or us for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate, or due to findings of undesirable effects caused by a biologically or mechanistically similar therapeutic or therapeutic candidate;
- delays in adding new investigators or clinical trial sites, or withdrawal of clinical trial sites from a study;
- failure by our CROs, clinical trial sites or patients, or other third parties, or us to adhere to clinical study requirements, including regulatory, contractual or protocol requirements;
- failure to perform in accordance with the GCP requirements, or applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements, policies and guidance that require amending or submitting new clinical protocols to regulatory authorities and IRBs, conducting additional studies, implementation of other changes that alter the data requirements or standards for obtaining regulatory approval, and other regulatory changes which may cause delays in our development programs, or changes to regulatory review times;
- there may be regulatory questions or disagreements regarding interpretations of data and results, or new information may emerge regarding our product candidates;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical studies of our product candidates being greater than we anticipate, or we may have insufficient funds for a clinical trial or to pay the substantial user fees required by the FDA upon the filing of an NDA;
- clinical trials of our product candidates producing negative or inconclusive results may fail to provide sufficient data and information to support product approval, or our clinical trials may fail to reach the necessary level of statistical or clinical significance, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials, or preclinical studies, or abandon product development programs;
- interruption of, or delays in receiving, supplies of our product candidates or other drugs or components of our therapies due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- early results from our clinical trials of our product candidates may be negatively affected by changes in efficacy measures, such as overall response rate and duration of response, as more patients are enrolled in our clinical trials or as new cohorts of our clinical trials are tested, and overall response rate and duration of response may be negatively affected by the inclusion of unconfirmed responses in preliminary results that we report if such responses are not later confirmed;
- we may not be able to demonstrate that a product candidate provides an advantage over current standards of care or current or future competitive therapies in development;
- there may be changes to the therapeutics or their regulatory status, which we are administering in combination with our product candidates;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or our manufacturing facilities for clinical and future commercial supplies;
- the FDA or comparable regulatory authorities may take longer than we anticipate making a decision on our product candidates;

- transfer of our manufacturing processes to our CMOs or other larger-scale facilities operated by a CMO or by us and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process;
- our use of different manufacturing processes within our clinical trials, and any effects that may result from the use of different processes on the clinical data that we have reported and will report in the future;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing, including as a result of any quality issues associated with the CMO; and
- business interruptions, changes in export regulation and controls, trade restrictions with companies based in certain countries, such as Russia or China, and other domestic and foreign regulations or restrictions resulting from geopolitical actions or national security concerns, including war, regional conflicts, terrorism, or natural disasters.

We also may conduct clinical and preclinical research in collaboration with other academic, pharmaceutical and biotechnology entities in which we combine our technologies with those of our collaborators. Such collaborations may be subject to additional delays because of the management of the trials, contract negotiations, the need to obtain agreement from multiple parties and the necessity of obtaining additional approvals for therapeutics used in the combination trials. These combination therapies will require additional testing and clinical trials will require additional FDA regulatory approval and will increase our future cost of expenses.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing changes to our product candidates, we may be required to, or we may elect to, conduct additional studies to bridge our modified product candidates to earlier versions. These changes may require FDA approval or notification and may not have their desired effect. The FDA may also not accept data from prior versions of the product to support an application, delaying our clinical trials or programs or necessitating additional clinical trials or preclinical studies. We may find that this change has unintended consequences that necessitates additional development and manufacturing work, additional clinical trials and preclinical studies, or that results in refusal to file or non-approval of an NDA.

Clinical trial delays could shorten any periods during which our product candidates have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. The number and types of preclinical studies and clinical trials that will be required for regulatory approval also vary depending on the product candidate, the disease or condition that the product candidate is designed to address and the regulations applicable to any particular product candidate. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that any product candidates we may seek to develop in the future will never obtain the appropriate regulatory approvals necessary for us or any future collaborators to commence product sales. Any delay in completing development or obtaining, or failing to obtain, required approvals could also materially adversely affect our ability or that of any of our collaborators to generate revenue from any such product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

In addition to U.S. regulatory requirements, we are also subject to regulation by foreign regulatory authorities, ethics committees, and other governmental entities with respect to clinical trials we conduct or sponsor outside of the U.S. For example, the EU Clinical Trials Regulation, or CTR, became applicable on January 31, 2022, repealing the EU Clinical Trials Directive. The implementation of the CTR also includes the implementation of the Clinical Trials Information System, a new clinical trial portal and database that will be maintained by the EMA in collaboration with the European Commission and the EU Member States. Complying with changes in regulatory requirements can incur additional costs, delay our clinical development plans, or expose us to greater liability if we are slow or unable to adapt to changes in existing requirements or new requirements or policies governing our business operations, including our clinical trials.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences, which could harm our business, financial condition, results of operations, and prospects significantly.

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, adverse events or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us, IRBs, Drug Safety Monitoring Boards, or DSMBs, or the FDA or comparable foreign regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Even if we were to receive product approval, such approval could be contingent on inclusion of unfavorable information in our product labeling, such as limitations on the indicated uses for which the products may be marketed or distributed, a label with significant safety warnings, including boxed warnings, contraindications, and precautions, a label without statements necessary or desirable for successful commercialization, or requirements for costly post marketing testing and surveillance, or other requirements, including a Risk Evaluation and Mitigation Strategy, or REMS, to monitor the safety or efficacy of the products, and in turn prevent us from commercializing and generating revenues from the sale of our current or future product candidates.

If unacceptable toxicities or side effects arise in the development of our product candidates, IRBs, DSMBs or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials, order our clinical trials to be placed on clinical hold, or deny approval of our product candidates for any or all targeted indications. The FDA or comparable foreign regulatory authorities may also require additional data, clinical, or pre-clinical studies if unacceptable toxicities arise. We may need to abandon development or limit development of that product candidate to certain 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. Toxicities associated with our clinical trials and products may also negatively impact our ability to conduct clinical trials in larger patient populations, such as in patients that have not yet been treated with other therapies or have not yet progressed on other therapies.

Treatment-emergent adverse events could also affect patient recruitment or the ability of enrolled subjects to complete our clinical trials or could result in potential product liability claims. Potential side effects associated with our product candidates may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from our product candidates may not be normally encountered in the general patient population and by medical personnel. Any of these occurrences could harm our business, financial condition, results of operations, and prospects significantly.

In addition, even if we successfully advance our product candidates or any future product candidates through clinical trials, such trials will only include a limited number of patients and limited duration of exposure to our product candidates. As a result, we cannot be assured that adverse effects of our product candidates will not be uncovered when a significantly larger number of patients are exposed to the product candidate after approval. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of using our product candidates over a multi-year period.

If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by such products or products with similar mechanism of action, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- we may be required to conduct additional clinical trials or post-approval studies;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication 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 implement a REMS or create a Medication Guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers and/or other elements to assure safe use;

- we could be sued and held liable for harm caused to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- the product may become less competitive; and
- our reputation may suffer.

In particular, following the FDA's review of a large randomized safety clinical trial of tofacitinib, a JAK inhibitor approved for the treatment of rheumatoid arthritis and UC, the FDA has determined there is an increased risk of serious heart-related events such as heart attack or stroke, blood clots, cancer and death associated with Xeljanz and Xeljanz XR (tofacitinib), and has issued black box warnings for certain JAK inhibitors in the same drug class as Xeljanz, including Olumiant (baricitinib) and Rinvoq (upadacitinib). The FDA approved Sotyktu (deucravacitinib), a TYK2 inhibitor, on September 9, 2022. While the FDA did not require a black box warning in Sotyktu's label, if the FDA considers other TYK2 inhibitors, a member of the JAK family, to have similar safety concerns as other JAK inhibitors, or if new data indicate potential safety concerns with TYK2 inhibitors, then the FDA may issue black box warnings for TYK2 inhibitors, which may limit market acceptance of VTX958, our lead TYK2 inhibitor, if approved, and could negatively impact the future commercial prospects of VTX958.

If any of the foregoing events occur, it could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, if one or more of our product candidates prove to be unsafe, our entire pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

The manufacturing of our product candidates is complex, and we may encounter difficulties in production, particularly with respect to process development, quality control, and scaling-up of our manufacturing capabilities. If we or our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to achieve and maintain a commercially viable cost structure.

Currently, our product candidates are manufactured using processes developed by our third-party CMOs that we may not intend to use for more advanced clinical trials or commercialization. We may ultimately be unable to reduce the cost of goods for our product candidates to levels that will allow for an attractive return on investment if and when those product candidates are commercialized.

Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. If our CMOs should cease manufacturing for us, we would experience delays in obtaining sufficient quantities of our product candidates for clinical trials and, if approved, commercial supply. Further, our CMOs may breach, terminate or not renew these agreements. If we were to need to find alternative manufacturing facilities it would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. The commercial terms of any new arrangement could be less favorable than our existing arrangements and the expenses relating to the transfer of necessary technology and processes could be significant.

Reliance on third-party manufacturers entails exposure to risks to which we would not be subject if we manufactured the product candidate ourselves, including:

- inability to negotiate manufacturing and quality agreements with third parties under commercially reasonable terms;
- reduced day-to-day control over the manufacturing process for our product candidates as a result of using third-party manufacturers for all aspects of manufacturing activities;
- reduced control over the protection of our trade secrets, know-how and other proprietary information from misappropriation or inadvertent disclosure or from being used in such a way as to expose us to potential litigation;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may be costly or damaging to us or result in delays in the development or commercialization of our product candidates; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any problems or delays we or our CMOs experience in preparing for commercial scale manufacturing of a product candidate may result in a delay in the FDA approval of the product candidate or may impair our ability to manufacture commercial quantities or such quantities at an acceptable cost, which could result in the delay, prevention or impairment of clinical development and commercialization of our product candidates and could adversely affect our business. Furthermore, if our product candidates are approved and we or our commercial manufacturers fail to deliver the required commercial quantities of our product candidates on a timely basis and at reasonable costs, we would likely be unable to meet demand for our products and we would lose potential revenues, which would adversely affect our business, financial condition, results of operations, and prospects.

In addition, the manufacturing process and facilities for any product candidates that we may develop is subject to FDA and foreign regulatory authority approval processes, and we or our CMOs will need to meet all applicable FDA and foreign regulatory authority requirements, including cGMP, on an ongoing basis. The cGMP requirements include quality control, quality assurance and the maintenance of records and documentation. The FDA and other regulatory authorities enforce these requirements through facility inspections. Manufacturing facilities must submit to pre-approval inspections by the FDA that will be conducted after we submit our marketing applications, including our NDAs, to the FDA. Manufacturers are also subject to continuing FDA and other regulatory authority inspections following marketing approval. Further, we, in cooperation with our CMOs, must supply all necessary chemistry, manufacturing and quality control documentation in support of an NDA on a timely basis. There is no guarantee that we or our CMOs will be able to successfully pass all aspects of a pre-approval inspection by the FDA or other foreign regulatory authorities.

Our CMOs' manufacturing facilities may be unable to comply with our specifications, cGMP, or with other FDA, state, and foreign regulatory requirements. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of product candidate that may not be detectable in final product testing. If we or our CMOs are unable to reliably produce products to specifications acceptable to the FDA or other regulatory authorities, or in accordance with the strict regulatory requirements, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs 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. Deviations from manufacturing requirements may further require remedial measures that may be costly and/or time-consuming for us or a third party to implement and may include the temporary or permanent suspension of a clinical trial or, if approved, commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business, financial condition, results of operations, and prospects.

Even to the extent we use and continue to use CMOs, we are ultimately responsible for the manufacture of our products and product candidates. A failure to comply with these requirements may result in regulatory enforcement actions against our manufacturers or us, including fines and civil and criminal penalties, which could result in imprisonment, suspension or restrictions of production, injunctions, delay or denial of product approval or supplements to approved products, clinical holds or termination of clinical trials, warning or untitled letters, regulatory authority communications warning the public about safety issues, refusal to permit the import or export of the products, product seizure, detention, or recall, operating restrictions, suits under the civil False Claims Act, corporate integrity agreements, consent decrees, or withdrawal of product approval.

Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and prospects.

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.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent

discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will likely expect to be granted rights to publish data arising out of such collaboration and any joint research and development programs may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Small molecule therapeutics rely on the availability of reagents, intermediates, specialized equipment and other specialty materials, which may not be available to us on acceptable terms or at all. For some of these reagents, intermediates, specialized equipment and other specialty materials, we rely or may rely on sole source vendors or a limited number of vendors, which could impair our ability to manufacture and supply our product candidates.

Manufacturing our product candidates requires many reagents, which are substances used in our manufacturing processes to bring about chemical reactions, intermediates, specialized equipment and other specialty materials, some of which are manufactured or supplied by small companies with limited resources and experience to support commercial production. We currently depend on a limited number of vendors for certain intermediates, specialized equipment and other specialty materials used in the manufacture of our product candidates. Some of these suppliers may not have the capacity to support clinical trials and commercial products manufactured under cGMP or may otherwise be ill-equipped to support our needs. Accordingly, we may experience delays in receiving key intermediates, materials and equipment to support clinical or commercial manufacturing.

For some of these reagents, intermediates, equipment and materials, we currently rely and may in the future rely on sole source vendors or a limited number of vendors. An inability to continue to source product from any of these suppliers, which could be due to a number of issues, including regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a supplier, labor disputes or shortages, unexpected demands or quality issues, could adversely affect our ability to satisfy demand for our product candidates. If our product candidates are approved, such inability to source product from our suppliers could adversely and materially affect our product sales and operating results or our ability to conduct clinical trials, either of which could significantly harm our business. As we continue to develop and scale our manufacturing process, we expect that we will need to obtain rights to and supplies of certain reagents, intermediates, equipment and materials to be used as part of that process. We may not be able to obtain rights to such reagents, intermediates, equipment and materials on commercially reasonable terms, or at all, and if we are unable to alter our process in a commercially viable manner to avoid the use of such reagents, intermediates, equipment or materials or find a suitable substitute, it would have a material adverse effect on our business. Even if we are able to alter our process so as to use other reagents, intermediates, equipment or materials, such a change may lead to a delay in our clinical development and, if approved, commercialization plans. If such a change occurs for a product candidate that is already in clinical testing, the change may require us to perform comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials, which may cause delays in our clinical development and commercialization plans.

Changes in the manufacturing process or formulation may result in additional costs or delay.

As product candidates progress through preclinical studies 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 planned clinical trials or other future 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. If we or our CMOs are not able to successfully manufacture our product candidates in sufficient quality and quantity, clinical development and timelines for our product candidates and subsequent approval could be adversely impacted.

We will be unable to commercialize our products if our clinical trials are not successful.

Our research and development programs are at an early stage. We must demonstrate our products' safety and efficacy in humans through extensive clinical testing. We may experience numerous unforeseen events during, or as a result of, the clinical testing process that could delay or prevent commercialization of our products, including but not limited to the following:

- safety and efficacy results in various human clinical trials reported in scientific and medical literature may not be indicative of results we obtain in our clinical trials;
- after reviewing test results, we or our collaborators may abandon projects that we might previously have believed to be promising;
- we, our collaborators or regulators may suspend or terminate clinical trials if the participating subjects or patients are being exposed to unacceptable health risks;
- the standard of care may change as the result of new technology or therapies in our target clinical indications, precluding regulatory approval or limited commercial use if approved;
- the effects our product candidates have may not be the desired effects or may include undesirable side effects or other characteristics that preclude regulatory approval or limit their commercial use if approved;
- manufacturers may not meet the necessary standards for the production of the product candidates or may not be able to supply the product candidates in a sufficient quantity; and
- regulatory authorities may find that our clinical trial design or conduct does not meet the applicable approval requirements.

Clinical testing is very expensive, can take many years and the outcome is uncertain. The data collected from our clinical trials may not be sufficient to support approval by the FDA of our product candidates for the treatment of inflammatory diseases and autoimmune disorders. The clinical trials for our product candidates under development may not be completed on schedule and the FDA may not ultimately approve any of our product candidates for commercial sale. If we fail to adequately demonstrate the safety and efficacy of any product candidate under development, we may not receive regulatory approval for such product candidate, which would prevent us from generating revenues or achieving profitability.

We may use our limited financial and human resources to pursue a particular type of treatment, or treatment for a particular type of disease, and fail to capitalize on programs or treatments of other types of diseases that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and human resources, we must choose to pursue and fund the development of specific types of treatment, or treatment for a specific type of disease, and may forego or delay pursuit of opportunities with other programs, investigational medicines, or treatment for other types of diseases, which could later prove to have greater commercial potential. Moreover, given the rapidly evolving competitive landscape and the time it takes to advance a product through clinical development, an incorrect decision to pursue a particular type of treatment or disease may have a material adverse effect on our results of operation and negatively impact our future clinical strategies. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for investigational medicines or clinical trials may not yield any commercially viable products. If we do not accurately evaluate and anticipate the commercial potential or target market for a particular type of treatment or disease, we may choose to spend our limited resources on a particular treatment, or treatment for a particular type of disease, and then later learn that another type of treatment or disease that we previously decided not to pursue would have been more advantageous. 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. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may develop product candidates in combination with other therapies, which exposes us to additional risks and could result in our products, even if approved, being removed from the market or being less successful commercially.

We may develop product candidates in combination with one or more other therapies. Even if any product candidate we develop 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 or comparable foreign regulatory authorities could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, even if approved, being removed from the market or being less successful commercially.

We also may choose to evaluate product candidates in combination with one or more therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval. If the FDA or comparable foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy.

The use of our net operating loss carryforwards may be limited.

Our net operating loss carryforwards may expire and not be used. As of December 31, 2023, we had U.S. federal net operating loss carryforwards of approximately $30.4 million. Our U.S. federal net operating loss carryforwards arising in taxable years beginning after December 31, 2017, are not subject to expiration under the Internal Revenue Code of 1986, as amended, or the "Code". The deductibility of U.S. federal net operating losses arising in taxable years beginning after December 31, 2017, is limited to 80% of our current year taxable income. Additionally, our ability to use any net operating loss carryforwards to offset taxable income in the future will also be limited under Section 382 of the Code, if we undergo an "ownership change" (generally defined as a cumulative change in ownership by "5-percent shareholders" of more than 50% within a rolling three-year period).

We may have experienced ownership changes in the past and, although we do not believe that we experienced an ownership change in connection with our listing on the Nasdaq Global Select Market, any such ownership change could result in increased future tax liability. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo ownership changes in the future. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. Furthermore, since we will need to raise substantial additional funding to finance our operations, we may undergo ownership changes in the future. Any such annual limitation may significantly reduce the utilization of the net operating loss carryforwards before they expire. Depending on our future tax position, limitation of our ability to use net operating loss carryforwards in jurisdictions in which we are subject to income tax could have an adverse impact on our results of operations and financial condition.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses by certain jurisdictions, including in order to raise additional revenue to help counter the fiscal impact from the COVID-19 pandemic, possibly with retroactive effect, or other unforeseen reasons, our existing net operating losses could expire or otherwise be unavailable to offset future income tax liabilities.

We may experience fluctuations in our tax obligations and effective tax rate, which could materially affect our results.

We are subject to income- and non-income-based taxes in the United States under federal, state, and local jurisdictions and in certain foreign jurisdictions in which we operate. Tax laws, regulations and administrative practices in various jurisdictions may be subject to significant change, with or without advance notice, due to economic, political and other conditions, and significant judgment is required in evaluating and estimating our provision and accruals for these taxes. Our effective tax rates could be affected by numerous factors, such as changes in tax, accounting and other laws, regulations, administrative practices, principles and interpretations, the mix and level of earnings in a given taxing jurisdiction or our ownership or capital structures.

For example, U.S. federal income tax legislation signed into law in 2017 referred to as the Tax Cuts and Jobs Act, is highly complex, is subject to interpretation, and contains significant changes to U.S. tax law, including, but not limited to, a reduction in the corporate tax rate, significant additional limitations on the deductibility of interest, substantial revisions to the taxation of international operations, and limitations on the use of certain net operating losses. Beginning in 2022, the Tax Cuts and Jobs Act eliminated the option to deduct research and development expenditures currently and requires taxpayers to capitalize and amortize them over five or fifteen years pursuant to Section 174 of the Code.

In addition, in 2022, the Inflation Reduction Act of 2022 (the "IRA"), was signed into law, with tax provisions primarily focused on implementing a 15% minimum tax on global adjusted financial statement income, effective for tax years beginning after December 31, 2022, and a 1% excise tax on share repurchases occurring after December 31, 2022. It is unclear at this time what, if any, impact the IRA will have on our tax rate and financial results. We will continue to evaluate the IRA's impact (if any) as further information becomes available.

Our international operations subject us to potentially adverse tax consequences.

We generally conduct our international operations through subsidiaries and report our taxable income in various jurisdictions worldwide based upon our business operations in those jurisdictions. Our intercompany relationships are subject to complex transfer pricing regulations administered by taxing authorities in various jurisdictions. The relevant taxing authorities may disagree with our determinations as to the value of assets sold or acquired or income and expenses attributable to specific jurisdictions. If such a disagreement were to occur, and our position were not sustained, we could be required to pay additional taxes, interest and penalties, which could result in one-time tax charges, higher effective tax rates, reduced cash flows, and lower overall profitability of our operations.

There is also a high level of uncertainty in today's tax environment stemming from both global initiatives put forth by the Organisation for Economic Co-operation and Development, or the OECD, and unilateral measures being implemented by various countries due to a lack of consensus on these global initiatives. As an example, the OECD has put forth two proposals—Pillar One and Pillar Two—that revise the existing profit allocation and nexus rules (profit allocation based on location of sales versus physical presence) and ensure a minimal level of taxation, respectively. The Council of the European Union has adopted the global corporate 15% minimum tax as provided for in Pillar Two and has directed EU member states to implement legislation enacting Pillar Two by December 31, 2023. Further, unilateral measures such as digital services tax and corresponding tariffs in response to such measures are creating additional uncertainty. If these proposals are passed, it is possible that we will have to pay higher taxes in countries where such rules are applicable.

Our projections regarding the market opportunities for our product candidates may not be accurate, and the actual market for our products may be smaller than we estimate.

We do not have verifiable internal marketing data regarding the potential size of the commercial market for our product candidates, nor have we obtained current independent marketing surveys to verify the potential size of the commercial markets for our current product candidates or any future product candidates. Since our current product candidates and any future product candidates will represent novel approaches to treating various conditions, it may be difficult, in any event, to accurately estimate the potential revenues from these product candidates. Accordingly, we may spend significant capital trying to obtain approval for product candidates that have an uncertain commercial market. Our projections of both the number of people who have inflammatory diseases and autoimmune disorders we are targeting, as well as the subset of people with these diseases who are in a position to receive second- or third- line therapy, and 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 by third parties, and may prove to be incorrect. Further, new studies or approvals of new therapeutics may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates and may also be limited by the cost of our treatments and the reimbursement of those treatment costs by third-party payors. Even if we obtain significant market share for our product candidates, because the potential target populations may be small, we may never achieve profitability without obtaining regulatory approval for additional indications.

Because our current product candidates represent, and our other potential product candidates will represent, novel approaches to the treatment of disease, there are many uncertainties regarding the development, the market acceptance, third-party reimbursement coverage and the commercial potential of our product candidates.

There are many uncertainties related to development, marketing, reimbursement and the commercial potential for our product candidates. There can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety and efficacy of our product candidates, or that the data generated in these clinical trials will be acceptable to the FDA to support marketing approval. The FDA may take longer than usual to come to a decision on any NDA that we submit and may ultimately determine that there is not enough data, information or experience with our product candidates to support an approval decision. The FDA may also require that we conduct additional post-marketing studies or implement risk management programs, such as REMS, until more experience with our product candidates is obtained. Finally, after increased usage, we may find

that our product candidates do not have the intended effect, do not work with other combination therapies or have unanticipated side effects, potentially jeopardizing initial or continuing regulatory approval and commercial prospects.

There is no assurance that our product candidates will gain broad acceptance among doctors or patients or that governmental agencies or third-party medical insurers will be willing to provide reimbursement coverage for proposed product candidates. The market for any product candidates that we develop, if approved, will also depend on the cost of the product candidate. We do not yet have sufficient information to reliably estimate what it will cost to commercially manufacture our current product candidates, and the actual cost to manufacture these products could materially and adversely affect the commercial viability of these products. Unless we can reduce manufacturing costs to an acceptable amount, we may never be able to develop a commercially viable product. If we do not successfully develop and, if approved, commercialize products based upon our approach or find suitable and economical sources for materials used in the production of our products, we will not become profitable, which would materially and adversely affect the value of our common stock, our business, financial condition, results of operations, and prospects.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates, if approved.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products, if approved. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection laws. Large judgments have also been awarded in class action lawsuits based on therapeutics that had unanticipated side effects. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our product candidates, if approved. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products, if approved;
- injury to our reputation or significant negative media attention;
- withdrawal of clinical trial participants or sites and potential termination of clinical trial sites or entire clinical programs;
- initiation of investigations by regulators, refusal to approve marketing applications or supplements, and withdrawal or limitation of product approvals;
- costs to defend litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- decrease in the price of our stock and overall value of our company;
- exhaustion of our available insurance coverage and our capital resources; or
- the inability to commercialize our product candidates.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we may develop, alone or with corporate collaborators. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. While we have obtained clinical trial insurance for our clinical trials, we may have to pay amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. 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.

Public opinion and scrutiny of immunology treatments may impact public perception of our company and product candidates, or may adversely affect our ability to conduct our business and our business plans.

Public perception may be influenced by claims, such as claims that our product candidates are unsafe, unethical or immoral and, consequently, our approach may not gain the acceptance of the public or the medical community. Negative public reaction to new immunology treatments in general could result in greater government regulation and stricter labeling requirements of products to treat inflammatory diseases and autoimmune disorders, including any of our product candidates, if approved, and could cause a decrease in the demand for any product candidates we may develop. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing, and their patients being willing to receive, treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. More restrictive government regulations or negative public opinion could have an adverse effect on our business, financial condition, results of operations and prospects, and may delay or impair the development and, if approved, commercialization of our product candidates or demand for any products we may develop.

We may be unable to establish effective marketing and sales capabilities or enter into agreements with third parties or related parties to market and sell our product candidates, if they are approved, and as a result, we may be unable to generate product revenues.

We currently do not have a commercial infrastructure for the marketing, sale and distribution of products. If approved, in order to commercialize our products, we must build our marketing, sales and distribution capabilities or make arrangements with third parties to perform these services, which will take time and require significant financial expenditures and we may not be successful in doing so. There are risks involved with establishing our own marketing and sales capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have incurred these commercialization expenses prematurely or unnecessarily. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Even if we are able to effectively establish a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing our current or future product candidates. To the extent we rely on third parties to commercialize any products for which we obtain regulatory approval, we would have less control over their sales efforts and could be held liable if they failed to comply with applicable legal or regulatory requirements.

We have little to no prior experience in the marketing, sale and distribution of biopharmaceutical products, and there are significant risks involved in the building and managing of a commercial infrastructure. The establishment and development of commercial capabilities, including a comprehensive healthcare compliance program, to market any product candidates we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our collaborators, will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, manage and retain medical affairs, marketing, sales and commercial support personnel. In the event we are unable to develop a commercial infrastructure, we may not be able to commercialize our current or future product candidates, which would limit our ability to generate product revenues. Factors that may inhibit our efforts to commercialize our current or future product candidates and generate product revenues include:

- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our current or future product candidates;
- our inability to effectively oversee a geographically dispersed sales and marketing team;
- the costs and time associated with the initial and ongoing training of sales and marketing personnel on legal and regulatory compliance matters and monitoring their actions;
- an inability to secure adequate coverage and reimbursement by government and private health plans;
- intense competition in the clinical indications for which the products are approved and any restrictions on the scope of claims that we may make for the products;
- limitations or warnings, including distribution or use restrictions, contained in the products' approved labeling;

- any distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory REMS or voluntary risk management plan;
- liability for sales or marketing personnel who fail to comply with the applicable legal and regulatory requirements;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization or engaging a contract sales organization; and
- if a health epidemic or other outbreak, such as COVID-19 occurs, it may negatively impact our ability to establish commercial operations, educate and interact with healthcare professionals, and successfully launch our product on a timely basis.

If our product candidates, if approved, do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

We have never commercialized a product candidate for any indication. Even if our product candidates are approved by the appropriate regulatory authorities for marketing and sale, they may not gain acceptance among physicians, patients, third-party payors and others in the medical community. If any product candidate for which we obtain regulatory approval does not gain an adequate level of market acceptance, we may not generate sufficient product revenues or become profitable. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. The degree of market acceptance of any of our product candidates will depend on a number of factors, some of which are beyond our control, including:

- the safety and efficacy of our product candidates;
- the prevalence and severity of adverse events associated with our product candidates;
- the clinical indications for which the products are approved and the approved claims that we may make for the products;
- limitations or warnings contained in the product's FDA-approved labeling, including potential limitations or warnings for such products that may be more restrictive than other competitive products;
- distribution and use restrictions imposed by the FDA with respect to such product candidates or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan;
- changes in the standard of care for the targeted indications for such product candidates;
- the relative difficulty of administration of such product candidates;
- cost of treatment as compared to the clinical benefit in relation to alternative treatments or therapies;
- the availability of adequate coverage and reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid;
- the extent and strength of our marketing and distribution of such product candidates;
- the safety, efficacy and other potential advantages of, and availability of, alternative treatments already used or that may later be approved for any of our intended indications;
- the timing of market introduction of such product candidates, as well as competitive products;
- the reluctance of physicians to switch their patients' therapeutics;
- the reluctance of patients to switch from their existing therapeutics regardless of the safety and efficacy of newer therapeutics;
- our ability to offer such product candidates for sale at competitive prices;

- the extent and strength of our third-party manufacturer and supplier support;
- adverse publicity about our product or favorable publicity about competitive products; and
- potential product liability claims.

Our efforts to educate the medical community and third-party payors as to the benefits of our product candidates may require significant resources and may never be successful. Even if the medical community accepts that our product candidates are safe and effective for their approved indications, physicians and patients may not immediately be receptive to such product candidates and may be slow to adopt them as an accepted treatment of the approved indications. If our current or future product candidates are approved, but do not achieve an adequate level of acceptance among physicians, patients, and third-party payors, we may not generate meaningful revenues from our product candidates and may never become profitable.

Our product candidates may face competition sooner than anticipated.

For small molecular product candidates, the Federal Food, Drug, and Cosmetic Act, or FDCA, provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for a generic version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. As such, we may face competition from generic versions of our small molecule product candidates, which will negatively impact our long-term business prospects and marketing opportunities.

We will need to obtain FDA approval of any proposed branded product names, and any failure or delay associated with such approval may adversely affect our business.

Any name we intend to use for our product candidates in the United States will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt alternative names for our product candidates. If we adopt alternative names, we will lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe or otherwise violate the existing rights of third parties, and be acceptable to the FDA. We may be unable to build a successful brand identity for a new product name in a timely manner or at all, which would limit our ability to commercialize our product candidates.

We are dependent on information technology, systems, infrastructure and data. Our internal computer systems, or those used by our CROs, CMOs, clinical sites or other contractors or consultants, may fail or suffer security breaches, which could result in a material adverse effect, including without limitation, a material operational or service interruption, harm to our reputation, significant fines, penalties and liability, breach or triggering of data protection laws, or loss of customers or sales.

We are dependent upon information technology systems, infrastructure and data. In the ordinary course of our business, we directly or indirectly collect, use, generate, transfer, disclose, maintain, dispose of, or otherwise process (collectively, "Process" or "Processing") sensitive data, including intellectual property, confidential information, preclinical and clinical trial data, proprietary business information, personal data and personally identifiable health information of our clinical trial subjects and employees, in our data centers and on our networks, or on those of third-party service providers. The secure Processing of this information is critical to our operations. Our obligations under applicable laws, regulations, contracts, industry standards, and other documentation may include maintaining the confidentiality, integrity, and availability of such data in our possession or control, maintaining reasonable and appropriate security safeguards as part of an information security program, and restrictions on the use and disclosure of such data. These obligations create potential liability to regulators, business partners, personnel, and other relevant stakeholders. The multitude and complexity of our computer systems and those of our CROs, CMOs, clinical sites or other contractors or consultants make them inherently vulnerable to service interruption or destruction, malicious intrusion attempts and other attacks, and random attacks. Security breaches or incidents,

whether resulting from inadvertent or intentional acts or omissions by third-party service providers, employees, contractors or others pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, business partners, or others could have been and may be exposed to unauthorized persons or to the public or otherwise lost, destroyed, altered, disclosed, disseminated, damaged, made unavailable or otherwise Processed without authorization.

Although we take measures designed to protect such information from unauthorized Processing, our internal computer systems and those of our CROs, CMOs, clinical sites and other contractors and consultants are vulnerable to cyberattacks, computer viruses, bugs or worms, and other attacks by computer hackers, cracking, application security attacks, social engineering, supply chain attacks and vulnerabilities through our third-party service providers, denial-of-service attacks (such as credential stuffing), extortion, and intentional disruptions of service; computer and network vulnerabilities or the negligence and malfeasance of individuals with authorized access to our information, failure or damage from natural disasters, terrorism, war, fire and telecommunication and electrical failures. Ransomware attacks, including those from organized criminal threat actors, nation-states and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, loss of data (including sensitive customer information), loss of income, significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the financial, operational and reputational impact of a ransomware attack, it may be preferable to make extortion payments, but we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments). Third parties may also attempt to fraudulently induce our employees, contractors, consultants, or third-party service providers into disclosing sensitive information such as usernames, passwords, or other information or otherwise compromise the security of our computer systems, networks, and/or physical facilities in order to gain access to our data. Cyberattacks are increasing in their frequency, sophistication and intensity. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups, such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. Additionally, some of our employees work remotely, which may pose additional data security risks. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts, or the efforts of our partners, vendors, CROs, CMOs, clinical sites and other contractors and consultants will prevent service interruptions, or identify breaches or incidents in our or their systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. Furthermore, we may not have adequate insurance coverage to protect us from, or adequately mitigate, liabilities or costs resulting from security breaches and incidents. 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.

If any such event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss or unauthorized modification or unavailability of clinical trial data from completed or ongoing clinical trials for a product candidate could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data, or may limit our ability to effectively execute a product recall, if required. We expect to incur significant costs in an effort to detect and prevent security breaches and incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach or incident. To the extent that any disruption or security breach or incident were to result in a loss of or damage to our data or applications, or the loss, destruction, alteration, prevention of access to, disclosure, or dissemination of, or damage or unauthorized access to, our data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal, confidential, or proprietary information) processed or maintained on our behalf, or any of these is perceived or believed to have occurred, we could incur liability and the further development of any product candidates could be delayed. Any such event or the perception that it has occurred, could also result in legal claims, demands, litigation or other proceedings by private actors, regulatory investigations or other proceedings, liability under laws that protect the privacy of personal information and significant regulatory penalties, injunctive relief, mandatory corrective action, and other remedies, and damage to our reputation and a loss of confidence in us and our ability to conduct clinical trials, which could delay the clinical development of our product candidates.

We face risks related to health epidemics and other outbreaks, such as COVID-19, which could significantly disrupt our operations or otherwise result in material adverse impacts to us.

Our business could be adversely impacted by the effects of health epidemics and other outbreaks, including:

- delays or difficulties in enrolling and retaining patients in our ongoing and planned clinical trials, and incurrence of additional costs as a result of any preclinical study and clinical trial delays and adjustments;

- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- shutdowns or continued business disruptions experienced by suppliers and other third parties with whom we conduct business;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption or delays of key clinical trial activities, such as clinical trial site monitoring and collecting sufficient clinical data, patient safety considerations or limitations on travel imposed or recommended by federal or state governments, employers and others;
- other limitations on resources that would otherwise be focused on the conduct of our business or our current or planned clinical trials or preclinical research, including because of sickness, the desire to avoid contact with large groups of people or government restrictions;
- delays in receiving approval from regulatory authorities to initiate our planned clinical trials;
- delays in receiving the supplies, materials and services needed to conduct clinical trials and preclinical research or to support manufacturing activities of our business and that of our suppliers or contractors;
- changes in clinical site policies and procedures for conducting clinical trials during the pandemic;
- changes in regulations as part of a response to health epidemics or other outbreaks which may require us to change the ways in which our clinical trials are conducted and incur unexpected costs, or require us to discontinue the clinical trials altogether; and
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors.

We are actively monitoring, evaluating, and responding to developments relating to COVID-19, including new strains of the disease that have emerged in certain locations, vaccination status both locally and globally, and changing restrictions on travel and other protocols as set forth by the Centers for Disease Control and Prevention and other government authorities. The extent to which COVID-19, including any variants that have emerged or may emerge in the future, or any other health epidemic impacts our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of a particular virus and its variants and the actions to contain it or treat its impact, among others. We cannot at this time quantify or forecast the business impact of COVID-19, and there can be no assurance that we will be able to avoid a material impact on our business, financial condition and operating results from the spread of COVID-19 or its consequences, including disruption to our business and downturns in business sentiment generally or in our industry. In addition, the COVID-19 pandemic increases the likelihood and potential severity of other risks described in the "Risk Factors" section. Although the COVID-19 national emergency ended on May 11, 2023, we can provide no assurance on the impact of any future public health concerns or related disruptions, including resurgence of COVID-19 cases, will have on our business or operations.

Our failure to comply with state, national and/or international data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

Numerous laws and legislative and regulatory initiatives at the federal and state levels address privacy and security concerns, and some state privacy laws apply more broadly than the Health Insurance Portability and Accountability Act, or HIPAA, and associated regulations. For example, California has enacted legislation—the California Consumer Privacy Act, or CCPA—which went into effect on January 1, 2020. The CCPA, among other things, creates new data privacy and security obligations for covered companies and provides new privacy rights to California consumers, including the right to opt out of certain disclosures of their information. The CCPA also provides for civil penalties as well as a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for certain information collected as part of clinical trials as specified in the law, it may regulate or impact our Processing of personal information depending on the context. Further, California voters approved the California Privacy Rights Act of 2020, or CPRA, in November 2020. The CPRA went into effect on January 1, 2023. The CPRA, among other things, gives California residents the ability to limit the use of their sensitive information, provides for penalties for CPRA violations concerning California residents under the age of 16, and establishes a new

California Privacy Protection Agency to implement and enforce the law. Other states, have considered or have enacted legislation addressing privacy and security. For example, Washington has enacted the My Health, My Data Act, which includes a private right of action. Additionally, numerous states, including Colorado, Virginia, Utah, Connecticut, Iowa, Indiana, Tennessee, Florida, Texas, Oregon, Delaware, and Montana, have considered or have enacted legislation similar to the CCPA and CPRA. These developments create the possibility for a patchwork of overlapping but different state laws, potentially resulting in further uncertainty and requiring us to incur additional costs and expenses in an effort to comply. We cannot yet determine the impact these laws and regulations or any future laws, regulations and standards may have on our business.

There are also various laws and regulations in other jurisdictions relating to privacy, data protection, and security. For example, the European Union, or EU, member states, the United Kingdom and other foreign jurisdictions, including Switzerland, have adopted data protection laws and regulations which impose significant compliance obligations on us. Moreover, the EU Data Protection Directive, which formerly governed the collection, Processing and other use of personal health or other data in the EU, was replaced with the EU General Data Protection Regulation, or the GDPR, in May 2018. The GDPR, which is wide-ranging in scope and applies extraterritorially, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to such individuals, the security and confidentiality of the personal data, data breach notification, the adoption of appropriate privacy governance, including policies, procedures, training and audits, and the use of third-party processors in connection with the Processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU, including to the U.S. In July 2020, in its Schrems II ruling, the Court of Justice of the EU invalidated the EU-U.S. Privacy Shield data transfer mechanism, limiting how organizations could lawfully transfer personal data from the EEA to the U.S. Other data transfer mechanisms such as the Standard Contractual Clauses approved by the European Commission have faced challenges in European courts (including being called into question in Schrems II), may require additional risk analysis and supplemental measures to be used, and may be challenged, suspended or invalidated. In addition, the European Commission provided updated versions of the Standard Contractual Clauses in June 2021 that are required to be implemented. These and other developments relating to cross-border transfers of personal data may cause us to have to make further expenditures on local infrastructure, limit our ability to Process personal data, change internal business processes or otherwise affect or restrict sales and operations. Notably, the GDPR provides an enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant entity, whichever is greater.

The United Kingdom implemented the Data Protection Act, effective May 2018 and statutorily amended in 2019, that contains provisions, including its own derogations, for application of the GDPR in the United Kingdom, and the United Kingdom has implemented a version of the GDPR referred to as the UK GDPR, which provides for fines of up to the greater of £17.5 million or 4% of annual global revenues. These developments could increase the risk of non-compliance and the costs of providing our products and services in a compliant manner. On June 28, 2021, the European Commission issued an adequacy decision in respect of the United Kingdom's data protection framework, allowing personal data transfers from EU member states to the United Kingdom to continue without requiring additional contractual or other measures in order to lawfully transfer personal data between the territories. This decision is subject to renewal after four years, however, and may be revisited by the European Commission at any time. The United Kingdom also has adopted updated standard contractual clauses, effective in March 2022, that are required to be implemented. We may incur substantial expense in complying with obligations under United Kingdom laws and regulations relating to privacy, data protection, and data security, and we may be required to make significant changes in our business operations, all of which may adversely affect our revenues and our business overall.

Complying with these numerous, complex and often changing regulations is expensive and difficult, and failure to comply with any privacy or data protection laws or data security laws or any security incident or breach involving the misappropriation, loss or other unauthorized Processing, use or disclosure of sensitive or confidential patient, consumer or other personal information, whether by us, one of our CROs or business associates or another third party, or the perception that any of these have occurred, could adversely affect our business, financial condition and results of operations, including but not limited to: costs associated with any investigation or other regulatory proceeding, or private claims or demands; material fines and penalties; compensatory, special, punitive and statutory damages; litigation; consent orders regarding our privacy and security practices; requirements that we provide notices, credit monitoring services and/or credit restoration services or other relevant services to impacted individuals; adverse actions against our licenses to do business; reputational damage; and injunctive relief. The recent implementation of the CCPA and GDPR has increased our responsibility and liability in relation to personal data that we process, including in clinical trials, and we may in the future be required to put in place additional mechanisms to ensure compliance with the CCPA, GDPR and other applicable laws and regulations, which could divert management's attention and increase our cost of doing business. In addition, new regulation or legislative actions regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. In this regard, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States,

the EU, the United Kingdom and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

We cannot assure you that our CROs or other third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches, which could have a corresponding effect on our business, including putting us in breach of our obligations under laws and regulations relating to privacy, data protection, or data security and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party Processing of such information. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition to our legal obligations, our contractual obligations relating to privacy, data protection and data security have become increasingly stringent. Furthermore, we may make numerous statements in our privacy policies and in our marketing materials providing assurances about the security of our data. If any of these statements prove to be untrue or are perceived as untrue, even through circumstances beyond our reasonable control, we may face claims, investigations or other proceedings by the U.S. Federal Trade Commission, state and foreign regulators, our customers and private litigants.

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 privacy and security practices or otherwise relating to any actual or perceived privacy or data security breach or incident, 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.

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

Competition for qualified personnel in the biotechnology and pharmaceuticals industry is intense due to the limited number of individuals who possess the skills and experience required. To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided, and plan to continue providing, equity incentive awards that vest over time. The value to employees of equity incentive awards 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. We face significant competition for employees, particularly scientific personnel, from other biopharmaceutical companies, which include both publicly traded and privately held companies, and we may not be able to hire new employees quickly enough to meet our needs. All of our employees are hired on an "at-will" basis, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. We may not be able to attract and retain quality personnel on acceptable terms, or at all, which may cause our business, financial conditions, results of operations and prospects to suffer.

Additionally, if we lose members of our senior management for a short or an extended time, we may not be able to find appropriate replacements on a timely basis, and our business could be adversely affected. Our existing operations and continued future development depend to a significant extent upon the performance and active participation of certain key individuals, including our chief executive officer, Dr. Raju Mohan.

Dr. Mohan, our chief executive officer, Mr. Krueger, our chief business officer, and Dr. Nuss, our chief scientific officer, have significant interests in other companies which may conflict with our interests.

Our chief executive officer, Dr. Mohan, serves as a Partner and Senior Advisor at New Science Ventures, and Dr. Mohan, Mr. Krueger, our chief business officer, and Dr. Nuss, our chief scientific officer, serve as officers of, and hold ownership interests in, Escalier Biosciences BV and Vimalan Biosciences, Inc. Escalier Biosciences and Vimalan Biosciences are in the business of discovering and developing therapies for the treatment of inflammatory diseases and autoimmune disorders. As a result, they or other companies affiliated with Dr. Mohan, Mr. Krueger and Dr. Nuss may compete with us for business opportunities or, in the future, develop products

that are competitive with ours (including products in other therapeutic fields which we may target in the future). As a result, the interests of Dr. Mohan, Mr. Krueger and Dr. Nuss may not be aligned with our other stockholders and they may from time to time be incentivized to take certain actions that benefit their other interests and that our other stockholders do not view as being in their interest as investors in our company. Moreover, even if they do not directly relate to us, actions taken by Dr. Mohan, Mr. Krueger and Dr. Nuss and the companies with which they are involved could impact us.

We will need to grow our size and capabilities, and we may experience difficulties in managing this growth, which could disrupt our operations.

Our operations are dependent upon the services of our executives and our employees who are engaged in research and development. The loss of the services of our executive officers or senior research personnel could delay our product development programs and our research and development efforts. In order to develop our business in accordance with our business plan, we will have to hire additional qualified personnel, including in the areas of research, manufacturing, clinical trials management, regulatory affairs, and sales and marketing. We are continuing our efforts to recruit and hire the necessary employees to support our planned operations in the near term. However, competition for qualified employees among companies in the biotechnology and biopharmaceutical industry is intense, and no assurance can be given that we will be able attract, hire, retain and motivate the highly skilled employees that we need. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

As of December 31, 2023, we had 79 full-time employees, compared to 58 full-time employees as of December 31, 2022. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our future financial performance and our ability to 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 a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain research and clinical development services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis, or at all, when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, compliance or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

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 on a timely basis, or at all.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We may evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses from time to time. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption or incurrence of additional indebtedness or contingent liabilities;
- dilution resulting from the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company or product, including difficulties associated with integrating new personnel;
- acquisition of intangible assets that could result in significant future amortization expenses;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

Depending on the size and nature of future strategic acquisitions, we may acquire assets or businesses that require us to raise additional capital or to operate or manage businesses in which we have limited experience. Making larger acquisitions that require us to raise additional capital to fund the acquisition will expose us to the risks associated with capital raising activities. Acquiring and thereafter operating larger new businesses will also increase our management, operating and reporting costs and burdens. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

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

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

We would face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

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

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay our development program or one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we

elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We expect to rely on third parties to perform many essential services for any products, if approved, that we commercialize, including services related to distribution, government price reporting, customer service, accounts receivable management, cash collection and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize our current or future product candidates, if any are approved, will be significantly impacted and we may be subject to regulatory sanctions.

We expect to retain third-party service providers to perform a variety of functions related to the sale of our current or future product candidates, if any are approved, key aspects of which will be out of our direct control. These service providers may provide key services related to distribution, customer service, accounts receivable management and cash collection. If we retain a service provider, we will substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action.

In addition, we may engage in the future with third parties to perform various other services for us relating to adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements related to adverse event reporting, then we could be subject to regulatory sanctions.

Additionally, we may contract in the future with a third party to calculate and report pricing information mandated by various government programs. If a third party fails to timely report or adjust prices as required or errs in calculating government pricing information from transactional data in our financial records, then it could impact our discount and rebate liability, and potentially subject us to regulatory sanctions or False Claims Act lawsuits.

We may not be able to obtain or maintain orphan drug designations for certain of our product candidates, and we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of greater than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the European Medicines Agency's, or the EMA's, Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. There can be no assurance that the FDA or the EMA's Committee for Orphan Medicinal Products will grant orphan designation for any indication for which we apply, or that we will be able to maintain such designation.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable exclusivity period is ten years in Europe, but such exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior, if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation

neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

In *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in *Catalyst*, FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst* order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

Risks Related to Government Regulation

The FDA regulatory approval process is lengthy, time-consuming and unpredictable, and we may experience significant delays in the clinical development and regulatory approval of our product candidates.

We have not previously submitted an NDA to the FDA, or similar approval filings to comparable foreign authorities. NDAs must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and efficacy for NDAs for each desired indication. Our current beliefs regarding the registration pathway for our product candidates are based on our interpretation of communications with the FDA to date and our efforts to address such communications, which may be incorrect. Further, enrollment in our trials may need to be further adjusted based on future feedback from the FDA or other regulatory agency input, which could result in significant delays to our currently anticipated timeline for development and approval of our product candidates or prevent their approval entirely.

We may also experience delays, including delays arising from the need to increase enrollment, in completing planned clinical trials for a variety of reasons, including delays related to:

- the availability of financial resources to commence and complete the planned clinical trials;
- reaching agreement on acceptable contract terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an IRB or central IRB;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a clinical trial;
- adding new clinical trial sites;
- manufacturing sufficient quantities of qualified materials under cGMP and applying them on a subject by subject basis for use in clinical trials; or
- timely implementing or validating changes to our manufacturing or quality control processes and methods needed to address FDA feedback.

We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, by the FDA or other regulatory authorities, or recommended for suspension or termination by DSMBs 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 or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product

revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

The clinical and commercial utility of our product candidates are uncertain and may never be realized.

Our product candidates are in clinical development. We are actively enrolling a Phase 2 trial of VTX958 in moderately to severely active Crohn's disease. We also recently reported topline results from a Phase 2 trial of VTX002 in patients with moderately to severely active UC, and activities are underway to support initiation of a Phase 3 trial of VTX002 in moderately to severely active UC during the second half of 2024. Additionally, we are conducting a Phase 2 trial of our peripheral NLRP3 inhibitor VTX2735 in patients with CAPS, and a Phase 1 trial of our novel CNS-penetrant NLRP3 inhibitor VTX3232 in adult healthy volunteers. Success in early clinical trials does not ensure that large-scale clinical trials will be successful nor does it predict final results. In addition, we will not be able to treat patients if we cannot manufacture a sufficient quantity of VTX958, VTX002, VTX2735, VTX3232 or other product candidates that meets our minimum specifications. In addition, VTX958, VTX002 and VTX2735 have only been tested in a small number of trial subjects. Results from these clinical trials may not necessarily be indicative of the safety and tolerability or efficacy of VTX958, VTX002 and VTX2735 as we expand into larger clinical trials. As noted above, to the extent the FDA considers any of our product candidates to share the same mechanism of action as other drug products with known safety concerns that warrant black box warnings, the FDA may require black box warnings for our product candidates, which would limit the market acceptance of our product candidates and negatively impact the future commercial prospects of our product candidates, if approved.

We may not ultimately be able to provide the FDA with substantial clinical evidence to support a claim of safety or efficacy sufficient to enable the FDA to approve our product candidates for any indication. This may be because later clinical trials fail to reproduce favorable data obtained in earlier clinical trials, because the FDA disagrees with how we interpret the data from these clinical trials or because the FDA does not accept these therapeutic effects as valid endpoints in pivotal clinical trials necessary for market approval. We will also need to demonstrate that our product candidates are safe. We do not have data on possible harmful long-term effects of our product candidates and do not expect to have this data in the near future. As a result, our ability to generate clinical safety and effectiveness data sufficient to support submission of a marketing application or commercialization of our product candidates is uncertain and is subject to significant risk.

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

In order to market and sell our products outside the United States, we or our third-party collaborators may be required to obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval policies and requirements may vary among jurisdictions. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval 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 studies 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 that we intend to charge for our products is also subject to approval. We or our collaborators may not be able to file for regulatory approval of our product candidates in international jurisdictions or obtain approvals from regulatory authorities outside the United States on a timely basis, if at all.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. If we fail to comply with the regulatory requirements in international markets and/or 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.

A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval of our product candidates outside of the U.S. and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other 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 taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems, and price controls;
- potential liability under the U.S. Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- the impact of public health epidemics on the global economy, such as the COVID-19 pandemic; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations.

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

We have never commercialized a product candidate, and we currently have no sales force, marketing or distribution capabilities. To achieve commercial success for the product candidates, which we may license to others, we will rely on the assistance and guidance of those collaborators. For product candidates for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party.

Factors that may affect our ability to commercialize our product candidates, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our approved product candidates, ensuring regulatory compliance of our company, employees and third parties under applicable healthcare laws and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of our product candidates upon approval. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may not generate revenues from them or be able to reach or sustain profitability.

We are, and if we receive regulatory approval of our product candidates, will continue to 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.

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of such product candidates. The FDA may also require a REMS to approve our product candidates, which could entail requirements for 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. The FDA may also require post-approval Phase 4 studies. Moreover, the FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the

FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may withdraw approval, require labeling changes, such as black box warnings, or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. Any such restrictions could limit sales of the product.

In addition, we, our contractors, and our collaborators are and will remain responsible for FDA compliance, including requirements related to product design, testing, clinical and pre-clinical trials approval, manufacturing processes and quality, labeling, packaging, distribution, adverse event and deviation reporting, storage, advertising, marketing, promotion, sale, import, export, submissions of safety and other post-marketing information and reports, such as deviation reports, registration, product listing, annual user fees and recordkeeping for our product candidates. We and any of our collaborators, including our contract manufacturers, could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with regulatory requirements. Application holders must further notify the FDA, and depending on the nature of the change, obtain FDA pre-approval for product and manufacturing changes. The cost of compliance with post-approval regulations may have a negative effect on our results of operations and financial condition.

Later discovery of previously unknown problems with our product candidates or safety concerns with other products in the same drug class or sharing the same mechanism of action as our product candidates, including adverse events of unanticipated severity or frequency, that the product candidate is less safe or effective than previously thought, problems with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing, distribution, or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- restrictions on the labeling of our product candidates, including required additional warnings, such as black box warnings, contraindications, precautions and restrictions on the approved indication or use;
- modifications to promotional pieces;
- changes to product labeling or the way the product is administered;
- liability for harm caused to patients or subjects;
- fines, restitution, disgorgement, warning letters, untitled letters or holds on or termination of clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates;
- injunctions or the imposition of civil or criminal penalties, including imprisonment;
- FDA debarment, debarment from government contracts, and refusal of future orders under existing contracts, exclusion from federal healthcare programs, consent decrees, or corporate integrity agreements;
- regulatory authority issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product candidate;
- reputational harm; or
- the product becoming less competitive.

Any of these events could further have other material and adverse effects on our operations and business and could adversely impact our stock price and could significantly harm our business, financial condition, results of operations, and prospects.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. In addition, if the Supreme Court reverses or curtails the *Chevron* doctrine, which gives deference to regulatory agencies in litigation against FDA and other agencies, more companies may bring lawsuits against FDA to challenge longstanding decisions and policies of FDA, which could undermine FDA's authority, lead to uncertainties in the industry, and disrupt FDA's normal operations, which could delay FDA's review of our marketing applications. We cannot predict the likelihood, nature or extent of government regulation that may arise from future 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 the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, be subject to other regulatory enforcement action, and we may not achieve or sustain profitability.

We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control. Exports of our product candidates outside of the United States must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our product candidates or changes in applicable export or import laws and regulations may create delays in the introduction, provision or sale of our product candidates in international markets, prevent customers from using our product candidates or, in some cases, prevent the export or import of our product candidates to certain countries, governments or persons altogether. Any limitation on our ability to export, provide or sell our product candidates could adversely affect our business, financial condition and results of operations.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, the USA PATRIOT Act and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We have used contract research organizations abroad for clinical trials. In addition, we may engage third-party intermediaries to sell our product candidates abroad once we enter a commercialization phase for our product candidates and/or to obtain necessary permits, licenses, and other regulatory approvals. We or our third-party intermediaries may have direct or indirect interactions with officials and employees of government agencies or state-owned or affiliated entities. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We have adopted an anti-corruption policy which mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. However, there can be no assurance that our employees and third-party intermediaries will comply with this policy or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other investigations or other enforcement actions. If such actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor, which can result in added costs and administrative burdens.

If we fail to comply with environmental, health, and safety laws and regulations, including regulations governing the handling, storage or disposal of hazardous materials, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous 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 materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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 or hazardous materials.

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 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.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA 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 payment of user fees and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the FDA, the Securities and Exchange Commission, or the SEC, and other government agencies on which our operations may rely is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies, including delays or disruptions due to staffing shortages, travel restrictions, or public health concerns, including resurgence of COVID-19 cases, 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. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns and disruptions could potentially impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

If we fail to comply with applicable federal and state healthcare laws, including FDA, healthcare fraud and abuse, pharmaceutical marketing and advertising, and information privacy and security laws, we could face substantial penalties and our business, financial condition, results of operations, and prospects could be adversely affected.

As a biopharmaceutical company, we, as well as any of our contractors who conduct business for or on our behalf, are subject to many federal and state healthcare laws, including the federal Anti-Kickback Statute, or AKS, the federal civil and criminal False Claims Act, or FCA, the Civil Monetary Penalties Statute, the Medicaid Drug Rebate statute and other price reporting requirements, the federal Physician Payment Sunshine Act, the Veterans Health Care Act of 1992, HIPAA (as amended by the Health Information Technology for Economics and Clinical Health Act), the U.S. Foreign Corrupt Practices Act of 1977, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2020, or collectively, the ACA, and similar state laws. Even though we do not make referrals of healthcare services or bill directly to Medicare, Medicaid, or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. If we do not comply with all applicable fraud and abuse laws, we may be subject to healthcare fraud and abuse enforcement by both the federal government and the states in which we conduct our business.

Laws and regulations require calculation and reporting of complex pricing information for prescription drugs, and compliance will require us to invest in significant resources and develop a price reporting infrastructure, or depend on third parties to compute and report our drug pricing. Pricing reported to the Centers for Medicare & Medicaid Services, or CMS, must be certified. Non-compliant activities expose us to FCA risk if they result in overcharging agencies, underpaying rebates to agencies, or causing agencies to overpay providers.

If we or our operations are found to be in violation of any federal or state healthcare law, or any other governmental regulations that apply to us, we may be subject to significant penalties, including civil, criminal, and administrative penalties, damages, fines, disgorgement, debarment from government contracts, refusal of orders under existing contracts, exclusion from participation in U.S. federal or state health care programs, corporate integrity agreements and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including, but not limited to, exclusions from participation in government healthcare programs, which could also materially affect our business.

In particular, if we are found to have impermissibly promoted any of our product candidates, we may become subject to significant liability and government fines. We, and any of our collaborators, must comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA, Department of Justice, Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress, and the public. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product candidate is approved. If we are not able to obtain FDA approval for desired uses or indications for our product candidates, we may not market or promote our product candidates for those indications and uses, referred to as off-label uses, and our business may be adversely affected. We further must be able to sufficiently substantiate any claims that we make for our product candidates, including claims comparing our products candidates to other companies' products and must abide by the FDA's strict requirements regarding the content of promotion and advertising.

While physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, we are prohibited from marketing and promoting our product candidates for indications and uses that are not specifically approved by the FDA. These off-label uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biopharmaceutical companies concerning off-label use.

The FDA and other agencies actively enforce the laws and regulations regarding product promotion, particularly those prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted a product may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees of permanent injunctions under which specified promotional conduct is changed or curtailed. Thus, we and any of our collaborators will not be able to promote any product candidates we develop for indications or uses for which they are not approved. In the United States, engaging in the impermissible promotion of our product candidates, following approval, for off-label uses can also subject us to false claims and other litigation under federal and state statutes, including fraud and abuse and consumer protection laws, which can lead to significant civil and criminal penalties and fines, agreements with governmental authorities that materially restrict the manner in which we promote or distribute our product candidates and do business through, for example, corporate integrity agreements, suspension or exclusion from participation in federal and state healthcare programs, and debarment from government contracts and refusal of future orders under existing contracts. These false claims statutes include the FCA, which allows any individual to bring a lawsuit against a biopharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims or causing others to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government decides to intervene and prevails in the lawsuit, the individual will share in the proceeds from any fines or settlement funds. If the government declines to intervene, the individual may pursue the case alone. These FCA lawsuits against manufacturers of drugs and biologics have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements in the hundreds of millions or billions of dollars, pertaining to certain sales practices and promoting off-label uses. In addition, FCA lawsuits may expose manufacturers to follow-on claims by private payors based on fraudulent marketing practices. This growth in litigation has increased the risk that a biopharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, as well as criminal and civil penalties, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid, or other federal and state healthcare programs. If we or our future collaborators do not lawfully promote our approved product candidates, if any, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations and prospects.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal and state fraud laws may prove

costly. 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.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

In both domestic and foreign markets, sales of our product candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Obtaining coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance.

Government authorities and third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. If reimbursement is not available, or is available only to limited levels, our product candidates may be competitively disadvantaged, and we, or our collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or our collaborators, to establish or maintain a market share sufficient to realize a sufficient return on our or their investments. Alternatively, securing favorable reimbursement terms may require us to compromise pricing and prevent us from realizing an adequate margin over cost. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a 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.

Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our product candidates. Even if we obtain coverage for a given product candidate, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Moreover, the factors noted above have continued to be the focus of policy and regulatory debate that has, thus far, shown the potential for movement towards permanent policy changes; this trend is likely to continue, and may result in more or less favorable impacts on pricing. Patients are unlikely to use our product candidates, unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our product candidates.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Prices paid for a drug also vary depending on the class of trade. Prices charged to government customers are subject to price controls, including ceilings, and private institutions obtain discounts through group purchasing organizations. Net prices for drugs may be further reduced by mandatory discounts or rebates required by government healthcare programs and demanded by private payors. It is also not uncommon for market conditions to warrant multiple discounts to different customers on the same unit, such as purchase discounts to institutional care providers and rebates to the health plans that pay them, which reduces the net realization on the original sale.

In addition, federal programs impose penalties on manufacturers of drugs marketed under an NDA, in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. Regulatory authorities and third-party payors

have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of our collaborators to sell our product candidates profitably. These payors may not view our product candidates, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of our collaborators, or may not be sufficient to allow our product candidates, if any, to be marketed on a competitive basis. Cost control initiatives could cause us, or our collaborators, to decrease, discount, or rebate a portion of the price we, or they, might establish for our product candidates, which could result in lower than anticipated product revenues. If the realized prices for our product candidates, if any, decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer. Moreover, the recent and ongoing series of congressional hearings relating to drug pricing has presented heightened attention to the biopharmaceutical industry, creating the potential for political and public pressure, while the potential for resulting legislative or policy changes presents uncertainty.

Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. If payors subject our product candidates to maximum payment amounts or impose limitations that make it difficult to obtain reimbursement, providers may choose to use therapies, that are less expensive when compared to our product candidates. Additionally, if payors require high copayments, beneficiaries may decline prescriptions and seek alternative therapies. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals and other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We, and our collaborators, cannot be sure that coverage will be available for any product candidate that we, or they, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we obtain marketing approval could have a material adverse effect on our results of operations, our ability to raise capital needed to commercialize products, and our overall financial condition.

There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

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

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

We are subject to new legislation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance, and adversely affect our ability to market our products, obtain collaborators and raise capital.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability, or the ability of our collaborators, to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our collaborators, may receive for any approved product candidates.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, in June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and healthcare measures initiated by the Biden administration will impact the ACA, our business, financial condition and results of operations. Complying with any new legislation or change in regulatory requirements could be time-intensive and expensive, resulting in a material adverse effect on our business.

Additional federal and state healthcare reform measures may be adopted in the future that may result in more rigorous coverage criteria, increased regulatory burdens and operating costs, decreased net revenue from our biopharmaceutical products, decreased potential returns from our development efforts, and additional downward pressure on the price that we receive for any approved drug. For example, the American Rescue Plan of 2021 eliminated the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. Further any reduction in reimbursement from Medicare or other government healthcare 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 product candidates.

Legislative and regulatory proposals may also be made to expand post-approval requirements and restrict sales and promotional activities for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the 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.

In addition, there have been a number of other policy, legislative and regulatory proposals aimed at changing the pharmaceutical industry, including heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, U.S. Congressional inquiries and proposed 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, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. In an effort to curb Medicare Patients' out-of-pocket costs for prescription drugs, the Part D redesign legislation requires manufacturers to contribute to the catastrophic coverage phase for Part D drugs, as discounts through a manufacturer discount program. Furthermore, any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. Various industry stakeholders, including certain pharmaceutical companies and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. The impact of these judicial challenges and any future legislative, executive, and administrative actions and agency rules implemented by the government on us and the biopharmaceutical industry as a whole is unclear. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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. For example, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. Further, FDA recently authorized the state of Florida to import certain prescription drugs from Canada for a period of two years to help reduce drug costs, provided that Florida's Agency for Health Care Administration meets the requirements set forth by the FDA. Other states may follow Florida. Any reduction in reimbursement from Medicare or other government programs may result in a reduction in payments from private payors.

We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The ACA and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. There can be no assurance that our product candidates will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available, or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

If our employees, independent contractors, consultants, commercial partners or vendors engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, we, directly or indirectly, could be exposed to significant losses and liability, including, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.

We are exposed to the risk of fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws of the FDA and other similar foreign regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed 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, structuring and commissions, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials.

We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter misconduct or other improper activities by our employees or third parties that we engage for our business operations, including independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our, or our employees', consultants', collaborators', contractors', or vendors' business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, compliance agreements, withdrawal of product approvals, and curtailment of our operations, among other things, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, we may not be able to compete effectively or operate profitably.

We rely upon a combination of patents, know-how and confidentiality agreements to protect the intellectual property related to our product candidates and to prevent third parties from copying and surpassing our achievements, thus eroding our competitive position in our market.

Our success is dependent in large part on our obtaining, maintaining, protecting and enforcing patents and other proprietary rights in the United States and other countries with respect to our product candidates and on our ability to avoid infringing the intellectual property and other proprietary rights of others. Furthermore, patent law relating to the scope of claims in the biotechnology field in which we operate is still evolving and, consequently, patent positions in our industry may not be as strong as in other more well-established fields. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date.

We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates and novel discoveries that are important to our business. Our pending and future patent applications may not result in patents being issued or issued patents may not afford sufficient protection of our product candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive products.

Obtaining and enforcing patents is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications or maintain and/or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Composition of matter patents for pharmaceutical product candidates often provide a strong form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our pending patent applications directed to composition of matter of our product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. 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 products for our targeted indications, physicians may prescribe these products "off-label." 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 prosecute.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. For example, 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. Patent applications in the United States and 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 make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, inventorship, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending patent applications may be challenged in patent offices in the United States and abroad. Even issued patents may later be found invalid or unenforceable or may be modified or

revoked in proceedings instituted by third parties before various patent offices or in courts. For example, our pending patent applications may be subject to third-party pre-issuance submissions of prior art to the USPTO or our issued patents may be subject to post-grant review (PGR) proceedings, oppositions, derivations, reexaminations, or inter partes review (IPR) proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. 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 products, or limit the duration of the patent protection of our product candidates. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such candidates are commercialized. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Any failure to obtain or maintain patent protection with respect to our product candidates or their uses could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. However, trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know-how, and if the license is not available on commercially-viable terms, then we may not be able to launch our product candidate. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries 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, we will not be able to establish or maintain a competitive advantage in our market, and this scenario could materially adversely affect our business, financial condition and results of operations.

We cannot ensure that patent rights relating to inventions described and claimed in our pending patent applications will issue or that patents based on our patent applications will not be challenged and rendered invalid and/or unenforceable.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. We have pending U.S. and foreign patent applications in our portfolio; however, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will 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 enforce and/or defend our patent rights which will be costly whether we win or lose;
- whether the patent applications that we own will result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries; and/or
- whether we may experience patent office interruption or delays to our ability to timely secure patent coverage to our product candidates.

We cannot be certain that the claims in our pending patent applications directed to our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries. There can be no assurance that any such patent applications will issue as granted patents. 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. Even if the patents do issue based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our product candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

We may not be able to protect our intellectual property rights throughout the world.

Patents are of national or regional effect, and although we currently have an issued patent and pending applications in the United States, filing, prosecuting and defending patents on all of our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These competitor products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Various companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many countries do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights.

Various countries outside the United States have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. As a result, a patent owner may have limited remedies in certain circumstances, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. 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.

Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. As such, we do not know the degree of future protection that we will have on our product candidates. While we will endeavor to try to protect our product candidates with intellectual property rights, such as patents, as appropriate, the process of obtaining patents is time consuming, expensive and unpredictable.

In addition, geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to the military conflict in Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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 or permit us to maintain our competitive advantage. For example:

- others may be able to make product candidates that are similar to ours, but that are not covered by the claims of the patents that we own;
- we or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own;
- we or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that noncompliance with the USPTO and foreign governmental patent agencies requirement for a number of procedural, documentary, fee payment and other provisions during the patent process can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own may be revoked, modified or held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own will result in issued patents with claims directed to our product candidates or uses thereof in the United States or in other foreign countries;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

If any of these or similar events occur, then they could significantly harm our business, results of operations and prospects.

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

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. There can be no assurance that our operations do not, or will not in the future, infringe existing or future third-party patents. Identification of third-party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration 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.

Numerous U.S. and foreign patents and pending patent applications exist in our market that are owned by third parties. 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. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Patent applications in the United States and elsewhere are typically 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. Certain U.S. applications that will not be filed outside the U.S. can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These patent applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our product candidates.

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. For example, we may incorrectly determine that our product candidates 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. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our research programs, product candidates, their respective methods of use, manufacture and formulations thereof, and could result 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.

We may be involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors or other third parties may infringe our patents, trademarks or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention, or decide that the other party's use of our patented technology falls under the safe harbor to patent infringement under 35

U.S.C. §271(e)(1). An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. 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. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third-party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders, or it may be otherwise impractical or undesirable to enforce our intellectual property against some third parties. Our competitors or other third parties may be able to sustain the costs of complex patent litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology or other product candidates, or enter into development partnerships that would help us bring our product candidates to market.

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 products candidates. We cannot be certain that our product candidates 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. We may decide in the future to seek a license to those third-party intellectual property patents, but we might not be able to do so on reasonable terms. 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. 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. 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, 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 current or future 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, could be found to be infringed by 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 or methods of use 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-exam, inter partes review or post-grant review proceedings. 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 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.

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. 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. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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 patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of a patent. The USPTO and various foreign governmental patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance 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, our competitors might be able to enter the market with similar or identical products, which would have a material adverse impact on our business, financial condition, results of operations and prospects.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first-to-file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either file any patent application related to our product candidates or other technologies or invent any of the inventions claimed in our patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Further, because of a lower evidentiary standard in these USPTO post-grant proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned patent applications and the enforcement or defense of our owned issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Additionally, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. While we do not believe that any of the patents owned by us will be found invalid based on the foregoing, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents.

In addition, as of June 1, 2023, European patent applications and patents may be subject to the jurisdiction of the European Unified Patent Court (UPC). Further, European patent applications will have the option, upon grant of a patent, of becoming a Unitary Patent, which will be subject to the jurisdiction of the UPC. The establishment of the UPC and Unitary Patent are significant changes in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any

litigation in the UPC. As the UPC, as a single court system, can invalidate a European patent, we, where applicable, have opted out of the UPC and as such, each European patent would need to be challenged in each individual country.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies, including our competitors or potential competitors. We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

We may not be able to license or acquire new or necessary intellectual property rights or technology from third parties.

Other parties, including our competitors, may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these patents, we may find it necessary or prudent to obtain licenses to such patents from such parties. The licensing or acquisition of intellectual property rights is a competitive area, and several 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. No assurance can be given that we will be successful in licensing any additional rights or technologies from third parties. Our inability to license the rights and technologies that we have identified, or that we may in the future identify, could have a material adverse impact on our ability to complete the development of our product candidates or to develop additional product candidates. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. Failure to obtain any necessary rights or licenses may detrimentally affect our planned development of our current or future product candidates and could increase the cost, and extend the timelines associated with our development, of such other product candidates, and we may have to abandon development of the relevant program or product candidate. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. 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 product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent. A patent term extension (PTE) 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 PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous PTEs 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 PTE 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.

We may become 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 patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. 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.

Our inventors may have performed work for other portfolio companies as part of their employment with Kalika Biosciences, Inc., or Kalika. While Kalika previously had a services agreement in place with each of its portfolio companies, which included the segregation of services and ownership of intellectual property for each portfolio company, including the ability of inventors to assign inventions, work product and intellectual property directly to us, disputes about ownership between us and Kalika and/or other portfolio companies of Kalika may arise in the future, which may have a material adverse effect on our business.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our reliance on third parties can also present intellectual property-related risks. For example, collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property-related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property. Collaborators may also own or co-own intellectual property covering our product candidates that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates. Collaborators may also gain access to our trade secrets or formulations and impact our ability to commercialize our product candidates. We may also need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us.

We may rely on trade secrets and proprietary know-how which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our product candidates, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Elements of our product candidates, including processes for their preparation and manufacture, may involve proprietary know-how, information or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. 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. 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 and know-how can be difficult to protect. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We and any third parties with whom we share facilities enter into written agreements that include confidentiality and intellectual property obligations to protect each party's potential trade secrets, proprietary know-how and information. We further seek to protect our potential trade secrets, proprietary know-how and information in part, by entering into non-disclosure and confidentiality agreements with parties who are given access to them, such as our corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. With our consultants, contractors and outside scientific collaborators, these agreements typically include invention assignment obligations. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. We cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Despite these 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. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. Further, 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. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third-party, our competitive position would be harmed.

We may be subject to claims that we or our employees, consultants or advisors have wrongfully used or disclosed alleged confidential information or trade secrets.

We have entered into and will enter in the future into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties. We may become subject to litigation where a third party asserts that we or our employees, consultants or advisors inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product or product candidates and technology. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business.

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

Our current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other 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 foreign 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. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively, and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Although these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

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. Similar requirements exist in Europe. 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, it 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. Furthermore, in many countries, 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. 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. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Risks Related to Our Common Stock

An active, liquid and orderly trading market may not be developed or sustained for our common stock, and, as a result, it may be difficult for you to sell your shares of our common stock.

The trading market for our common stock on the Nasdaq Global Select Market has been limited and an active trading market for our common stock may never develop or be sustained. If a market for our common stock does not develop or is not sustained, 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 and progression of our product pipeline may not meet 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.

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

The market price of our common stock is likely to be volatile and could fluctuate widely in response to many factors, including but not limited to:

- announcements of the results of clinical trials by us, our collaborators or our competitors, or positive or negative developments with respect to similar products, including those being developed by our collaborators or our competitors;
- volatility and instability in the financial markets and capital markets, including any impact of adverse developments effecting the financial services industry, such as those based on liquidity constraints or concerns;
- developments with respect to patents or proprietary rights;
- announcements of technological innovations by us or our competitors;
- announcements of new products or new contracts by us or our competitors;
- actual or anticipated variations in our operating results due to the level of development expenses and other factors;
- changes in financial estimates by equities research analysts and whether our earnings meet or exceed such estimates;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders, or the perception or anticipation thereof;
- expiration of market standoff or lock-up agreements;
- conditions and trends in the pharmaceutical, biotechnology and other industries;
- receipt, or lack of receipt, of funding in support of conducting our business;

- regulatory developments within, and outside of, the United States, including changes in the structure of health care payment systems;
- litigation or arbitration;
- natural disasters or major catastrophic events, such as the COVID-19 pandemic;
- general economic, political and market conditions and other factors; and
- the occurrence of any of the risks described in this "Risk Factors" section.

From December 31, 2022 until December 31, 2023, the closing price of our common stock has ranged from a low of $2.08 to a high of $46.65. In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance.

Additionally, a decrease in trading price of our common stock may cause our common stock to no longer satisfy the continued listing standards of Nasdaq. If we are not able to maintain the requirements for listing on Nasdaq, we could be delisted, which could have a materially adverse effect on our ability to raise additional funds as well as on the price and liquidity of our common stock.

Subject to various spending levels approved by our board of directors, our management will have broad discretion in the use of the net proceeds from our capital raises and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from our capital raises and our stockholders will not have the opportunity as part of their investment decision to assess whether the net proceeds from our capital raises are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from our capital raises, their ultimate use may vary substantially from their currently intended use. You may not agree with our decisions, and our use of the proceeds from our capital raises may not yield any return to stockholders. Our failure to apply the net proceeds of our capital raises effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of those net proceeds. Stockholders will not have the opportunity to influence our decisions on how to use our net proceeds from our capital raises. Pending their use, we may invest the net proceeds from our capital raises in interest and non-interest bearing cash accounts, short-term, investment-grade, interest-bearing instruments and U.S. government securities. These temporary investments are not likely to yield a significant return.

You may experience future dilution as a result of future equity offerings or other equity issuances.

We will have to raise additional capital in the future. To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may be lower than the price you paid per share. In addition, investors purchasing shares or other securities in the future could have rights superior to those of other investors. Any such issuance could result in substantial dilution to investors.

A sale of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of our common stock intend to sell shares, could reduce the market price of our common stock.

As of February 22, 2024, we had 59,252,349 outstanding shares of common stock. All of these shares are available for sale in the public market, subject to limitations under Rule 144 with respect to affiliates of our company.

On February 13, 2024, we filed a Post-Effective Amendment No. 1 to our shelf registration statement on Form S-3 with the Securities and Exchange Commission, to register the offering, sale and issuance of up to $100.0 million in aggregate of our common stock, preferred stock, debt securities, guarantees of debt securities, warrants and units from time to time in one or more offerings. This Post-Effective Amendment No. 1 was filed due to our expectation that we would cease to be a well-known seasoned issuer (as such term is defined in Rule 405 under the Securities Act) upon the filing of this Annual Report on Form 10-K.

Each time we offer to sell securities under the registration statement, we will provide a prospectus supplement that will contain specific information about the terms of that offering and the securities being offered.

For example, pursuant to the Form S-3, we may sell shares of common stock under our Sales Agreement with Jefferies, as sales agent, pursuant to which we could offer and sell, from time to time through Jefferies, shares of common stock providing for aggregate sales proceeds of up to $150.0 million. As of December 31, 2023, the Company has issued and sold 1,176,470 shares of common stock through the Sales Agreement.

In addition, we have filed registration statements on Form S-8 under the Securities Act registering the issuance of 18,077,251 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under the registration statements on Form S-8 can be freely sold in the public market upon issuance, subject to volume limitation applicable to affiliates and the lock-up agreements described above.

We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, could adversely affect the market price of our common stock.

Our board of directors is authorized to issue and designate shares of our preferred stock in additional series without stockholder approval.

Our amended and restated certificate of incorporation authorizes our board of directors, without the approval of our stockholders, to issue shares of our preferred stock, subject to limitations prescribed by applicable law, rules and regulations (including Nasdaq rules) and the provisions of our amended and restated certificate of incorporation, as shares of preferred stock in series, to establish from time to time the number of shares to be included in each such series and to fix the designation, powers, preferences and rights of the shares of each such series and the qualifications, limitations or restrictions thereof. The powers, preferences and rights of these additional series of preferred stock may be senior to or on parity with our common stock, which may reduce its value.

We do not anticipate paying cash dividends for the foreseeable future, and therefore investors should not buy our stock if they wish to receive cash dividends.

You should not rely on an investment in our common stock to provide dividend income. We have never declared or paid any cash dividends or distributions on our common stock. We currently intend to retain our future earnings to support operations and to finance expansion and, therefore, we do not anticipate paying any cash dividends on our common stock in the foreseeable future. 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.

Our existing directors and executive officers and related entities hold a significant portion of our common stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2023, our executive officers and directors and related entities beneficially owned a significant portion of our outstanding voting stock. These stockholders, acting together, may be able to impact matters requiring stockholder approval. For example, they may be able to impact the elections of directors, amendments to our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholder and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

There can be no assurance that we will be able to comply with the continued listing standards of Nasdaq.

If Nasdaq delists our shares of common stock from trading on its exchange for failure to meet Nasdaq's listing standards, we and our stockholders could face significant material adverse consequences including: a limited availability of market quotations for our securities; reduced liquidity for our securities; a determination that our common stock is a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules and possibly result in a reduced level of trading activity in the secondary

trading market for our securities; a limited amount of new and analyst coverage; and a decreased ability to issue additional securities or obtain additional financing in the future.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our amended and restated certificate of incorporation and amended and restated bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue shares of convertible preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change in our control;
- provide that the authorized number of directors may be changed only by resolution of the board of directors, subject to the rights of any holders of convertible preferred stock;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and also meet specific requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the board of directors, the chairman of the board of directors, our chief executive officer or president (in the absence of a chief executive officer); and
- provide that stockholders will be permitted to amend certain provisions of our bylaws only upon receiving at least two-thirds of the votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and bylaws could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another state court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for the following (except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court or for which such court does not have subject matter jurisdiction):

- any derivative action or proceeding brought on our behalf;

- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the Delaware General Corporation Law, our certificate of incorporation or our bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

Our amended and restated bylaws further provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. The enforceability of similar exclusive federal forum provisions in other companies' organizational documents has been challenged in legal proceedings, and while the Delaware Supreme Court has ruled that this type of exclusive federal forum provision is facially valid under Delaware law, there is uncertainty as to whether other courts would enforce such provisions and that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

These exclusive forum provisions may (i) increase the costs for an investor and/or (ii) limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find either exclusive forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could have a material adverse effect on our business, financial condition, and results of operations.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our certificate of incorporation and bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. In addition, as permitted by Section 145 of the Delaware General Corporation Law, our bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We are not obligated pursuant to our bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- The rights conferred in our bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

To the extent that a claim for indemnification is brought by any of our directors or officers, it would reduce the amount of funds available for use in our business.

General Risk Factors

If equities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our stock, our stock price and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If such coverage is not maintained, the market price for our stock may be adversely affected. Our stock price also may decline if any analyst who covers us issues an adverse or erroneous opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet analysts' expectations. If one or more analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline and possibly adversely affect our ability to engage in future financings.

Failure to establish and maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and if investors lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline significantly.

As a public company, we are required to comply with the SEC's rules implementing Sections 302 and 404 of the Sarbanes-Oxley Act, which requires management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of controls over financial reporting. Additionally, due to our loss of emerging growth company status as of December 31, 2023, our independent registered public accounting firm was required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 as of December 31, 2023.

We do not currently have any internal audit function. To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts.

Testing and maintaining internal control can divert our management's attention from other matters that are important to the operation of our business. Additionally, when evaluating our internal control over financial reporting, we may identify material weaknesses that we may not be able to remediate in time to meet the applicable deadline imposed upon us for compliance with the requirements of Section 404. If we identify any material weaknesses in our internal control over financial reporting or are unable to comply with the requirements of Section 404 in a timely manner or assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could be negatively affected, and we could become subject to investigations by the stock exchange on which our securities are listed, the SEC or other regulatory authorities, which could require additional financial and management resources. In addition, if we fail to remedy any material weakness, our financial statements could be inaccurate, and we could face restricted access to capital markets.

If a restatement of our financial statements were to occur, our stockholders' confidence in our financial reporting in the future may be affected, which could in turn have a material adverse effect on our business and stock price.

If any material weaknesses in our internal control over financial reporting are discovered or occur in the future, our consolidated financial statements may contain material misstatements, and we could be required to further restate our financial results. In addition, if we are unable to successfully remediate any future material weaknesses in our internal controls or if we are unable to produce accurate and timely financial statements, our stock price may be adversely affected, and we may be unable to maintain compliance with applicable stock exchange listing requirements.

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 provide reasonable assurance 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, 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.

Unfavorable global economic conditions, including 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 business, financial condition, results of operations, or prospects.

Our business, financial condition, results of operations or prospects could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, or additional global financial crises, could result in a variety of risks to our business, including weakened demand for our product candidates, if approved, or our inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

In addition, 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 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 us, the financial institutions with which we have 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. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

In addition, investor concerns regarding the U.S. 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.

Our operations are vulnerable to business disruptions, including events beyond our control, which could seriously harm operations and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. In addition, our corporate headquarters is located in San Diego County, California, near major earthquake faults and fire zones, and the ultimate impact on us for being located near major earthquake faults and fire zones and being consolidated in a certain geographical area is unknown. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

We incur significant costs as a result of being a public company, which may adversely affect our business, financial condition, results of operations, prospects, and the price of our common stock.

We incur costs associated with corporate governance requirements that are applicable to us as a public company, including rules and regulations of the SEC, under the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 (the Dodd-Frank Act), and the Securities Exchange Act of 1934, as amended (the Exchange Act), as well as the rules of Nasdaq. These rules and regulations can significantly increase our accounting, legal, insurance, financial compliance and other costs and make some activities more time consuming. 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. 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.

The Exchange Act requires us to file annual, quarterly and current reports with respect to our business and financial condition within specified time periods and to prepare a proxy statement with respect to our annual meeting of stockholders. The Sarbanes-Oxley Act requires that we maintain effective disclosure controls and procedures and internal controls over financial reporting. Upon the loss of our status as an emerging growth company as of December 31, 2023, we are no longer exempt from the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, and our independent registered public accounting firm will evaluate and report on the effectiveness of internal control over financial reporting. Nasdaq requires that we comply with various corporate governance requirements. To maintain and improve the effectiveness of our disclosure controls and procedures and internal controls over financial reporting and comply with the Exchange Act and Nasdaq requirements, significant resources and management oversight will be required. This may divert management's attention from other business concerns and lead to significant costs associated with compliance, which could have a material adverse effect on us and the price of our common stock.

The expenses incurred by public companies generally for reporting and corporate governance purposes have been increasing. We expect these laws and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly, although we are currently unable to estimate these costs with any degree of certainty. These laws and regulations could also make it more difficult or costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. These laws and regulations could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or its committees or as our executive officers. Advocacy efforts by stockholders and third parties may also prompt even more changes in governance and reporting requirements. We cannot predict or estimate the amount of costs we may incur or the timing of these costs. Furthermore, if we are unable to satisfy our obligations as a public company, we could be subject to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation. Accordingly, increases in costs incurred as a result of becoming a publicly traded company may adversely affect our business, financial condition, results of operations, and prospects.

We may be subject to securities litigation, which is expensive and could divert management attention.

Following periods of volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention and resources from our business, which could seriously harm our business.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Risk Management and Strategy

We have established policies and processes for assessing, identifying, and managing material risk from cybersecurity threats, and have integrated these processes into our overall risk management systems and processes. We routinely assess material risks from cybersecurity threats, including any potential unauthorized occurrence on or conducted through our information systems that may result in adverse effects on the confidentiality, integrity, or availability of our information systems or any information residing therein.

We conduct risk assessments on a recurring basis to identify cybersecurity threats, as well as assessments in the event of a material change in our business practices that may affect information systems that are vulnerable to such cybersecurity threats. These risk assessments include identification of reasonably foreseeable internal and external risks, the likelihood and potential damage that could result from such risks, and the sufficiency of existing policies, procedures, systems, and safeguards in place to manage such risks.

Following these risk assessments, we re-design, implement, and maintain reasonable safeguards to minimize identified risks; reasonably address any identified gaps in existing safeguards; and regularly monitor the effectiveness of our safeguards. We devote significant resources and designate high-level personnel, including our Chief Business Officer who reports to our Chief Executive Officer, to manage the risk assessment and mitigation process.

As part of our overall risk management system, we monitor and test our safeguards and train our employees on these safeguards, in collaboration with other members of senior management. Personnel at all levels and departments are made aware of our cybersecurity policies through trainings.

We engage consultants and other third parties in connection with our risk assessment processes. These service providers assist us to design and implement our cybersecurity policies and procedures, as well as to monitor and test our safeguards. We require each third-party service provider to certify that it has the ability to implement and maintain appropriate security measures, consistent with all applicable laws, to implement and maintain reasonable security measures in connection with their work with us, and to promptly report any suspected breach of its security measures that may affect our company.

As of December 31, 2023, and through the date of this filing, we are not aware of any material cybersecurity incidents that have impacted the Company. For additional information regarding whether any risks from cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to materially affect our company, including our business strategy, results of operations, or financial condition, please refer to Item 1A, “Risk Factors,” in this annual report on Form 10-K.

Governance

One of the key functions of our board of directors is informed oversight of our risk management process, including risks from cybersecurity threats. Our board of directors is responsible for monitoring and assessing strategic risk exposure, and our executive officers are responsible for the day-to-day management of the material risks we face. Our board of directors administers its cybersecurity risk oversight function directly as a whole, as well as through the audit committee.

Our Chief Business Officer and other members of senior management are primarily responsible to assess and manage our material risks from cybersecurity threats. We have engaged a third party, who authored security manuals and holds multiple industry certifications, as our Virtual Chief Information Security Officer (VCISO) to support our Head of IT in Cyber related architecture and assessment.

Our Chief Business Officer and other members of senior management oversee our cybersecurity policies and processes, including those described in “Risk Management and Strategy” above. The processes by which our Chief Business Officer and other members of senior management are informed about and monitor the prevention, detection, mitigation, and remediation of cybersecurity incidents includes the following: rollout and expansion of cyber security tools and cyber industry awareness and trends.

Our Chief Business Officer and other members of senior management provide quarterly briefings to the audit committee regarding our company’s cybersecurity risks and activities, including any recent cybersecurity incidents and related responses, cybersecurity systems testing, activities of third parties, and the like. Our audit committee provides regular updates to the board of directors on such reports. In addition, our Chief Business Officer provides annual briefings to the board of directors on cybersecurity risks and activities.

Item 2. Properties

We lease approximately 35,016 square feet of office space for our headquarters in San Diego, California. The corresponding lease has a term through July 2031.

We also lease 9,801 square feet of office space in Encinitas, California. The corresponding leases have terms through June 2026.

We also lease 2,153 square feet of office and laboratory space in Ghent, Belgium. The corresponding lease has a term through June 2024.

Management believes that the office and laboratory space is suitable and adequate to meet our anticipated near-term needs.

Item 3. Legal Proceedings

The information set forth in Note 5 "Commitments and Contingencies," to the Notes to Consolidated Financial Statements included in the accompanying audited consolidated financial statements of this Annual Report on Form 10-K, is incorporated herein by this reference.

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 for Common Stock

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VTYX".

Stockholders

As of February 22, 2024, we have 59,252,349 shares of common stock outstanding held by 19 holders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our capital stock, and we do not currently intend to pay any cash dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business. Any future determination related to dividend policy will be made at the discretion of our board of directors, subject to applicable laws, and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions and capital requirements.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by this Item regarding equity compensation plans is incorporated by reference to the information set forth in Part III, Item 12 of this Annual Report on Form 10-K.

Sales of Unregistered Securities

There were no sales of unregistered securities by us during the fourth quarter of 2023 that were not previously reported in our quarterly reports on Form 10-Q and current reports on Form 8-K filed with the SEC.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of financial condition and results of operations should be read together with our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. In addition to historical financial information, the following discussion and analysis and other parts of this Annual Report on Form 10-K contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, based upon current expectations that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part I, Item 1A (Risk Factors) of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel small molecule product candidates to address a range of inflammatory diseases with significant unmet need. We leverage the substantial experience of our team in immunology to identify important new targets and to develop differentiated therapeutics against these targets. Our clinical product candidates address therapeutic indications with substantial commercial opportunity for novel small molecules. We are developing VTX958, a selective allosteric tyrosine kinase type 2 (TYK2) inhibitor, for the treatment of moderately to severely active Crohn's disease. In the fourth quarter of 2023, we announced topline data from a Phase 2 trial of VTX958 in moderate to severe plaque psoriasis. While the study achieved its primary and key secondary endpoints, the efficacy results did not meet our internal target to support further development of VTX958 in psoriasis. Based on these results, we have elected to terminate ongoing activities in the Phase 2 trials of VTX958 in plaque psoriasis and psoriatic arthritis. We are also conducting a Phase 2 trial of VTX958 in moderately to severely active Crohn's disease, for which we expect to report topline results in the middle of 2024. In addition, we are developing VTX002, a sphingosine 1 phosphate receptor (S1P1R) modulator for the treatment of moderately to severely active ulcerative colitis (UC). In the fourth quarter of 2023, we announced positive results from the Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis. Additionally, activities are underway to support initiation of a Phase 3 trial of VTX002 in ulcerative colitis during the second half of 2024. We expect to initiate a Phase 3 trial of VTX002 in ulcerative colitis in 2024. Our third product candidate, VTX2735, is a peripheral-targeted NOD-like receptor protein 3 (NLRP3) inflammasome inhibitor. We are conducting a Phase 2 trial for VTX2735 in cryopyrin-associated periodic syndrome (CAPS) patients and continue to evaluate additional indications for clinical development. We expect to provide a data update from the Phase 2 trial of VTX2735 in CAPS during the first quarter of 2024. In addition to VTX2735, we are conducting a Phase 1 trial of VTX3232, our novel CNS-penetrant NLRP3 inhibitor, in healthy volunteers. We expect to provide a data update from the Phase 1 trial of VTX3232 during the first quarter of 2024.

We were incorporated in November 2018. To date, we have focused primarily on organizing and staffing our company, business planning, raising capital and identifying our product candidates and conducting preclinical studies and clinical trials. We have funded our operations primarily through equity and debt financings. We do not have any products approved for sale and have not generated any revenue from product sales.

We have incurred significant operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future. Our net losses were $193.0 million and $108.4 million for the years ended December 31, 2023 and December 31, 2022, respectively. We had an accumulated deficit of $419.2 million as of December 31, 2023. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on a variety of factors, including the timing and scope of our preclinical studies and clinical trials and our expenditures on other research and development activities.

We do not expect to generate any revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, until such time as we can generate substantial product revenues to support our cost structure, if ever, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional capital when needed, we could be forced to delay, limit, reduce or terminate our product candidate development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

September 2022 Private Placement

On September 20, 2022, we issued and sold 5,350,000 shares of common stock through a private placement to certain qualified institutional buyers and institutional accredited investors. The common stock had a purchase price of $33.00 per share for aggregate gross proceeds of approximately $176.6 million. We received approximately $165.2 million in net proceeds after deducting fees to the placement agents and other offering expenses payable by the Company.

ATM Sales Agreement

In December 2022, we entered into an Open Market Sales Agreement℠ (Sales Agreement) with Jefferies LLC (Jefferies), as sales agent, pursuant to which we could offer and sell, from time to time through Jefferies, shares of common stock providing for aggregate sales proceeds of up to $150.0 million. We have no obligation to sell any shares under the Sales Agreement, and could at any time suspend solicitations and offers under the Sales Agreement.

In February 2023, we issued and sold 1,176,470 shares of common stock through the Sales Agreement. The common stock had an average purchase price of $42.50 per share for aggregate gross proceeds of $50.0 million. We received approximately $48.4 million in net proceeds after deducting commissions and offering expenses payable by us.

Impact of Macroeconomic Factors

Economic uncertainty in various global markets, including the U.S. and Europe, caused by political instability and conflict, such as the military conflicts in Ukraine and the Middle East, and economic challenges caused by the COVID-19 pandemic, have led to market disruptions, including significant volatility in commodity prices, credit and capital market instability and supply chain interruptions, which have caused volatile changes to inflation globally. Our business, financial condition and results of operations could be materially and adversely affected by further negative impact on the global economy and capital markets resulting from these or future global economic conditions, particularly if such conditions are prolonged or worsen.

Although, to date, our business has not been materially impacted by these global economic and geopolitical conditions, it is impossible to predict the extent to which our operations will be impacted in the short and long term, or the ways in which such instability could impact our business and results of operations. The extent and duration of these market disruptions, whether as a result of the military conflicts in Ukraine and the Middle East and effects of related sanctions, geopolitical tensions, volatile changes to inflation or otherwise, are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this report.

Financial Operations Overview

Revenues

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products for the foreseeable future. We may also generate revenues in the future from payments or royalties associated with potential partnering or collaboration agreements, but have no plans to enter into such arrangements at this time.

Research and Development Expenses

Research and development expenses consist of expenses incurred while performing research and development activities to discover and develop our product candidates. Direct research and development costs include external research and development expenses incurred under agreements with contract research organizations, consultants and other vendors that conduct our preclinical and clinical activities, expenses related to manufacturing our product candidates for preclinical and clinical studies, laboratory supplies and license fees. Indirect research and development costs include personnel-related expenses, consisting of employee salaries, payroll taxes, bonuses, benefits and stock-based compensation charges for those individuals involved in research and development efforts. Costs incurred in our research and development efforts are expensed as incurred.

We typically use our employee, consultant and infrastructure resources across our research and development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or certain external consultant costs to specific product candidates or development programs. These costs are included in unallocated

research and development expenses. The following table summarizes research and development expenses by product candidate or development program (in thousands):

	Year ended December 31,	
	2023	2022
VTX958	$ 80,577	$ 29,328
VTX002	38,363	23,352
VTX2735	3,306	9,364
VTX3232	5,315	4,953
Unallocated research and development expenses	48,206	20,741
Total research and development expenses	$ 175,767	$ 87,738

Substantially all of our research and development expenses to date have been incurred in connection with the discovery and development of our product candidates. We expect our research and development expenses may increase in the future as we advance an increased number of our product candidates through clinical development, including the conduct of our ongoing and planned clinical trials. The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. The successful development of product candidates is highly uncertain and subject to numerous risks and uncertainties. Accordingly, at this time, we cannot reasonably estimate the nature, timing or costs required to complete the remaining development of any product candidates and to obtain regulatory approval for one or more of these product candidates.

The costs of clinical trials may vary significantly over the life of a project owing to, but not limited to, the following:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the clinical trials;
- the countries in which the clinical trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the clinical trials and the drop-out or discontinuation rates of such patients;
- the number of doses that patients receive;
- the cost of comparative agents used in clinical trials;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up;
- the efficacy and safety profile of the product candidate; and
- establishing clinical manufacturing capabilities or making arrangements with third-party manufacturers in order to ensure that we or our third-party manufacturers are able to make product successfully.

We do not expect any of our product candidates to be commercially available for the next several years, if ever.

General and Administrative Expenses

General and administrative expenses are related to legal and patent costs, finance, human resources and other administrative activities. These expenses consist primarily of legal expenses, personnel costs, including stock-based compensation expenses, outside services, management fees and other general and administrative costs.

We expect that our general and administrative expenses may increase in the future as we expand operations, increase our headcount to support our continued research and development activities and operate as a public reporting company (including increased fees for outside consultants, lawyers and accountants, as well as increased directors' and officers' liability insurance premiums). We have also

incurred, and expect to continue to incur, increased costs to comply with stock exchange listing and SEC requirements, corporate governance, internal controls, investor relations and disclosure and similar requirements applicable to public companies, particularly as we ceased to be an emerging growth company and smaller reporting company as of December 31, 2023. Additionally, if and when we believe that regulatory approval of a product candidate appears likely, we may incur significant increases in our general and administrative expenses related to the sales and marketing of any approved product candidate.

Results of Operations

Comparison of Years Ended December 31, 2023 and 2022

The following table summarizes our consolidated results of operations for the years ended December 31, 2023 and 2022 (in thousands):

	Year ended December 31,		
	2023	**2022**	**Change**
Operating expenses:			
Research and development (includes related party amounts of $1,023 and $883, respectively)	$ 175,767	$ 87,738	$ 88,029
General and administrative	32,227	25,398	6,829
Total operating expenses	207,994	113,136	94,858
Loss from operations	(207,994)	(113,136)	(94,858)
Other (income) expense:			
Interest income	(15,074)	(4,669)	(10,405)
Other (income) expense	42	(41)	83
Total other income	(15,032)	(4,710)	(10,322)
Net loss	$ (192,962)	$ (108,426)	$ (84,536)
Unrealized gain (loss) on marketable securities	1,121	(1,023)	2,144
Foreign currency translation	(48)	(42)	(6)
Comprehensive loss	$ (191,889)	$ (109,491)	$ (82,398)

Research and Development Expense

Research and development expenses were $175.8 million and $87.7 million for the years ended December 31, 2023 and 2022, respectively. For the year ended December 31, 2023, most research and development expenses have been related to the development of VTX958, VTX002 and VTX3232.

For the year ended December 31, 2023, as compared to the year ended December 31, 2022, there was a net increase in research and development expenses of approximately $88.0 million. This increase was comprised of increases in costs between periods associated with the Phase 1 and Phase 2 trials for VTX958 of approximately $51.2 million, the Phase 2 trial for VTX002 of approximately $15.0 million, and IND enabling studies and the Phase 1 trial for VTX3232 of approximately $0.4 million, offset by a decrease in costs associated with the Phase 1 and Phase 2 trials for VTX2735 of $6.1 million. There were also increases in stock-based compensation expense of approximately $8.0 million and compensation-related expenses of approximately $14.5 million. Additionally, approximately $5.0 million of the increase between periods was attributable to professional service fees incurred, non-program specific discovery costs, facility related costs, software license and support costs and travel costs.

General and Administrative Expense

General and administrative expenses were $32.2 million and $25.4 million for the years ended December 31, 2023 and 2022, respectively. The increase of $6.8 million was primarily due to increased personnel costs, including stock-based compensation of approximately $4.0 million, compensation-related expenses of approximately $2.6 million and professional service fees of approximately $0.9 million. These increases were offset by a decrease in insurance costs of approximately $0.6 million.

Other (Income) Expense

Other income was $15.0 million and $4.7 million for the years ended December 31, 2023 and 2022, respectively. During the year ended December 31, 2023, the other income recognized was associated with net accretion income and interest earned on our available-for-sale marketable securities and dividends received from our cash equivalents.

Liquidity and Capital Resources

Sources of Liquidity and Capital Resources

From inception through December 31, 2023, we have funded our operations primarily through the issuance of equity and debt securities. Prior to our initial public offering (IPO) in October 2021, we issued an aggregate of $164.2 million of convertible preferred stock, net of offering costs, to outside investors and related parties and $10.3 million in aggregate principal amount of convertible notes and SAFEs issued to related parties. In October 2021, we received net proceeds of approximately $158.8 million, after deducting underwriting discounts and commissions and offering expenses payable by us, from the sale of our shares of common stock in the IPO. In September 2022, through the closing of our private placement, we received net proceeds of approximately $165.2 million after deducting transaction-related expenses. In February 2023, we received approximately $48.4 million in net proceeds after deducting commissions and offering expenses payable by us from the sale of shares of our common stock through the Sales Agreement. As of December 31, 2023, we had cash, cash equivalents and marketable securities of $252.2 million, excluding restricted cash of $1.0 million.

We have not entered into any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Future Funding Requirements

To date, we have generated no revenue and do not expect to generate revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates and we do not know when, or if, this will occur. In addition, our expenses may significantly increase in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our product candidates. Moreover, we continue to incur additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of our product candidates, we may incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing operations. Our expenses may increase substantially if and as we:

- continue research and development, including preclinical and clinical development of our existing product candidates;
- seek regulatory approval for our product candidates;
- seek to discover and develop additional product candidates;
- establish a commercialization infrastructure and scale up our manufacturing and distribution capabilities to commercialize any of our product candidates for which we may obtain regulatory approval;
- seek to comply with regulatory standards and laws;
- maintain, leverage and expand our intellectual property portfolio;
- hire clinical, manufacturing, scientific and other personnel to support our product candidates;
- incur expenses related to development and future commercialization efforts;
- add personnel, financial and management information systems and personnel; and
- incur additional legal, accounting and other expenses in operating as a public company.

Based on our current business plan, we believe that existing cash, cash equivalents, and marketable securities will be sufficient to fund our obligations for at least twelve months from the issuance of these consolidated financial statements. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect.

We enter into contracts in the normal course of business with various third-party consultants, contract research organizations (CRO) and contract manufacturing organizations (CMO) for preclinical research, clinical trials and manufacturing activities. These contracts

generally provide for termination upon notice. Payments due upon cancellation consist of cancellation fees and payments for services provided or expenses incurred, including non-cancellable obligations of our service providers, up to the date of cancellation. Actual expenses associated with these arrangements may be higher or lower than anticipated due to various factors, including progress of our development candidates, enrollment in ongoing clinical trials, which may be competitive and challenging and results from our ongoing and planned clinical trials.

Short-term liquidity needs pertaining to our operating leases is approximately $2.2 million. Long-term liquidity needs pertaining to our operating leases is approximately $15.6 million with our last minimum lease payment due in July 2031. Currently, we have no short-term or long-term purchase commitments.

Our capital expenditures to date have been immaterial and we do not expect to incur significant costs related to capital expenditures in the short or long-term.

The successful development of any product candidate is highly uncertain. Due to the numerous risks and uncertainties associated with the development and commercialization of our product candidates, if approved, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development of our product candidates.

Our future capital requirements will depend on many factors, including:

- the timing of, and the costs involved in, preclinical and clinical development and obtaining any regulatory approvals for our product candidates;
- the costs of manufacturing, distributing and processing our product candidates;
- the number and characteristics of any other product candidates we develop or acquire;
- the degree and rate of market acceptance of any approved products;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing intellectual property claims, including litigation costs and the outcome of such litigation;
- the timing, receipt and amount of sales of, or royalties on, any approved products; and
- any product liability or other lawsuits related to our product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity, equity-linked and debt financings, collaborations, strategic alliances and/or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. 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 or declaring dividends. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with pharmaceutical partners, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

We have incurred net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. As of December 31 2023, we had cash, cash equivalents and marketable securities of $252.2 million, excluding restricted cash of $1.0 million.

The following table sets forth a summary of the net cash flow activity for each of the periods indicated:

	Year ended December 31,	
	2023	2022
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (166,522)	$ (98,771)
Investing activities	$ 100,940	$ (74,931)
Financing activities	$ 53,329	$ 167,772

Operating Activities

Net cash used in operating activities was $166.5 million for the year ended December 31, 2023 and was primarily due to our net loss of $193.0 million offset by $20.7 million for noncash items and a net increase of $5.8 million in operating assets and liabilities. The noncash items included approximately $28.6 million for stock-based compensation expense, approximately $1.0 million for the amortization of operating right-of-use assets and depreciation expense and approximately $0.3 million for the loss on impairment of the Encinitas ROU asset and associated furniture and fixtures, offset by approximately $9.2 million for the net accretion of investments in available-for-sale marketable securities. The $5.8 million change in operating assets and liabilities was primarily attributable to an increase in accrued expenses of approximately $6.0 million, a decrease in accounts payable of approximately $0.7 million, and a decrease in prepaid expenses and other assets of approximately $0.6 million, offset by a decrease in operating lease liabilities of approximately $0.1 million.

Net cash used in operating activities was $98.8 million for the year ended December 31, 2022 and was primarily due to our net loss of $108.4 million offset by $14.8 million for noncash items and a net decrease of $5.2 million in operating assets and liabilities. The noncash items included approximately $16.6 million for stock-based compensation expense and approximately $0.4 million for the amortization of operating right-of-use assets and depreciation expense, slightly offset by approximately $2.2 million for the net accretion/amortization of investments in available-for-sale marketable securities. The $5.2 million change in operating assets and liabilities was primarily attributable to an increase in accrued expenses and accounts payable of approximately $3.4 million, offset by an increase in prepaid expenses and other assets of approximately $8.3 million and a decrease in operating lease liabilities of approximately $0.3 million.

Investing Activities

Net cash provided by investing activities was $100.9 million for the year ended December 31, 2023 and was primarily related to $373.7 million in proceeds from maturities of available-for-sale marketable securities, offset by the purchase of $272.3 million of investments in available-for-sale marketable securities and purchases of property and equipment of approximately $0.5 million.

Net cash used in investing activities was $74.9 million for the year ended December 31, 2022 and was primarily related to the purchase of $347.2 million of investments in available-for-sale marketable securities, offset by $272.6 million in proceeds from maturities of available-for-sale marketable securities.

Financing Activities

Net cash provided by financing activities was $53.3 million for the year ended December 31, 2023 and was attributable to approximately $48.4 million in net proceeds from the issuance of common stock under the Sales Agreement, approximately $4.7 million in proceeds from the exercise of stock options and approximately $0.2 million in proceeds from the issuance of common stock under the 2021 Employee Stock Purchase Plan (2021 ESPP).

Net cash provided by financing activities was $167.8 million for the year ended December 31, 2022 and was attributable to approximately $165.4 million in net proceeds from the issuance of common stock from the private placement, $2.1 million in proceeds from the exercise of stock options, and $0.3 million in proceeds from the issuance of common stock under the 2021 ESPP.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to prepaid and accrued clinical trial and research and development costs, available-for-sale marketable securities, the measurement of operating lease right-of-use assets and operating lease liabilities and the measurement of the fair value of stock-based awards. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies and estimates to be most critical to the preparation of our consolidated financial statements.

Long-Lived Assets

We evaluate long-lived assets, including property, equipment and operating lease right-of-use (ROU) assets, for impairment whenever events or circumstances indicate that the carrying value of an asset or asset group may not be recoverable. We group assets at the lowest level for which cash flows are separately identified in order to measure an impairment. Events or circumstances that would result in an impairment review include a significant change in the use of an asset, the planned sale or disposal of an asset, or a projection or forecast that demonstrates continuing losses associated with the use of a long-lived asset or asset group. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of the asset to future undiscounted cash flows expected to be generated by the asset or asset group. If the asset or asset group is determined to be impaired, the impairment recognized is measured by the amount by which the carrying value of the asset or asset group exceeds its fair value.

Assumptions and estimates used to determine cash flows in the evaluation of impairment and fair values used to determine the impairment are subject to a degree of judgment and complexity. Any future changes to the assumptions and estimates resulting from changes in actual results or market conditions from those anticipated may affect the carrying value of long-lived assets and could result in additional impairment charges, and such changes could be material.

Accrued Clinical Trial and Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each consolidated balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued expenses as of each consolidated balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The significant estimates in our accrued clinical trial and research and development expenses include the costs incurred for services performed by our vendors in connection with clinical trial and research and development activities for which we have not yet been invoiced.

We base our expenses related to clinical trial and research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct clinical trials and research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical trial and research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future clinical trial or research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that

are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation Expense

Stock-based compensation expense represents the cost of the grant date fair value of equity awards recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. We estimate the fair value of equity awards using the Black-Scholes option pricing model and recognize forfeitures as they occur. Estimating the fair value of equity awards as of the grant date using valuation models, such as the Black-Scholes option pricing model, is affected by assumptions regarding a number of variables, including the risk-free interest rate, the expected stock price volatility, the expected term of stock options, the expected dividend yield and the fair value of the underlying common stock on the date of grant. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop. See Note 8 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted, if any, during the years ended December 31, 2023 and 2022.

Other Company Information

Transition from Emerging Growth Company and Smaller Reporting Company Status

On December 31, 2023, we ceased to be an "emerging growth company" ("EGC"), as defined in the JOBS Act, due to our large accelerated filer status. Accordingly, we may no longer take advantage of EGC-related reduced reporting requirements that are otherwise applicable to public companies. For example, we have previously elected to take advantage of the extended transition period for complying with new or revised accounting standards. EGC status also exempted us from having to provide an auditor attestation of internal control over financial reporting under Sarbanes-Oxley Act Section 404(b).

On December 31, 2023, we also ceased to be a "smaller reporting company" because the market value of our stock held by non-affiliates plus the aggregate amount of gross proceeds to us as a result of our initial public offering exceeded $700 million as of June 30, 2023. However, we are complying with certain scaled disclosure requirements available to smaller reporting companies in this Annual Report (including, for example, presenting only the two most recent fiscal years of audited consolidated financial statements), which we are permitted to do under SEC rules because we were a smaller reporting company in 2023. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

Due to the loss of EGC and smaller reporting company status, we expect our public company compliance costs to increase.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial positions, results of operations or cash flows is disclosed in Note 2 of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2023 and 2022, we had cash, cash equivalents and marketable securities of $252.2 million and $356.6 million, respectively, primarily invested in U.S. Treasury securities, U.S. government agency securities, corporate debt securities, commercial paper, asset-backed securities and money market accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term available-for-sale marketable securities. Our available-for-sale marketable securities are subject to interest rate risk and will fall in value if market interest rates increase.

We have limited exposure to foreign currency exchange rates and do not enter into foreign currency hedging transactions. The functional currency of certain foreign subsidiaries is the local currency. Accordingly, the effects of exchange rate fluctuations on the net assets of these foreign subsidiaries' operations are accounted for as translation gains or losses in accumulated other comprehensive loss within stockholders' equity. A hypothetical change of 100 basis points in such foreign currency exchange rates during the year ended December 31, 2023 would be immaterial.

Item 8. Financial Statements and Supplementary Data

The information required by this Item 8 is included in Part IV, Item 15 of this Annual Report on Form 10-K and is incorporated herein by reference.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(3) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of December 31, 2023, the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of the end of the period covered by this Annual Report on Form 10-K, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specific in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financing reporting, as such term is defined in Exchange Act Rule 13a-15(f). Internal control over financial reporting is a process to provide reasonable assurance regarding the reliability of our financial reporting for external purposes in accordance with U.S. generally accepted accounting principles. Internal control over financial reporting includes maintaining records that in reasonable detail accurately and fairly reflect our transactions; providing reasonable assurance that transactions are recorded as necessary for preparation of our consolidated financial statements; providing reasonable assurance that receipts and expenditures of company assets are made in accordance with management authorization; and providing reasonable assurance that unauthorized acquisition, use or disposition of company assets that could have a material effect on our consolidated financial statements would be prevented or detected on a timely basis. Because of its inherent limitations, internal control over financial reporting is not intended to provide absolute assurance that a misstatement of our consolidated financial statements would be prevented or detected.

Under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on the evaluation under this framework, our Chief Executive Officer and Chief Financial Officer have concluded that our internal control over financial reporting was effective as of December 31, 2023.

Attestation Report of the Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their attestation report herein, which expresses an unqualified opinion on the effectiveness of our internal control over financial reporting as of December 31, 2023.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Ventyx Biosciences, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Ventyx Biosciences, Inc.'s internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Ventyx Biosciences, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2023, and the related notes and our report dated February 27, 2024 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's 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 for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Diego, California
February 27, 2024

Item 9B. Other Information

Securities Trading Plans of Directors and Executive Officers

During our last fiscal quarter, the following directors and officers, as defined in Rule 16a-1(f), terminated a "Rule 10b5-1 trading arrangement" or a "non-Rule 10b5-1 trading arrangement," as defined in Regulation S-K Item 408, as follows:

On December 11, 2023, Martin Auster, M.D., our Chief Financial Officer, terminated a Rule 10b5-1 trading arrangement providing for the sale from time to time of an aggregate of 278,472 shares of our common stock. The trading arrangement was intended to satisfy the affirmative defense in Rule 10b5-1(c). The duration of the trading arrangement was until July 24, 2024, or earlier if all transactions under the trading arrangement are completed.

On December 14, 2023, William J. Sandborn, M.D., our former President and Chief Medical Officer, terminated a Rule 10b5-1 trading arrangement providing for the sale from time to time of an aggregate of 270,998 shares of our common stock. The trading arrangement was intended to satisfy the affirmative defense in Rule 10b5-1(c). The duration of the trading arrangement was until September 27, 2024, or earlier if all transactions under the trading arrangement are completed.

No other officers or directors, as defined in Rule 16a-1(f), adopted or terminated a "Rule 10b5-1 trading arrangement" or a "non-Rule 10b5-1 trading arrangement," as defined in Regulation S-K Item 408, during the last fiscal quarter.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspection

Not applicable.

PART III

We will file a definitive Proxy Statement for our 2024 Annual Meeting of Stockholders, or the 2024 Proxy Statement, with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2024 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

Item 10. Directors, Executive Officers and Corporate Governance

Except as set forth below, the information required by Item 10 is hereby incorporated by reference to the information contained in our definitive proxy statement for the 2024 annual meeting of stockholders.

Code of Business Conduct and Ethics

Our board of directors has adopted a Code of Business Conduct and Ethics that applies to all of our employees, officers and directors, including our Chief Executive Officer, Chief Financial Officer and other executive and senior financial officers. The full text of our Code of Business Conduct and Ethics is posted on the governance page on our website which is located at https://ir.ventyxbio.com/corporate-governance/documents-and-charters. We will post any amendments to our Code of Business Conduct and Ethics, or waivers of its requirements, on our website.

Item 11. Executive Compensation

The information required by Item 11 is hereby incorporated by reference to the information contained in our definitive proxy statement for the 2024 annual meeting of stockholders.

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

The information required by Item 12 is hereby incorporated by reference to the information contained in our definitive proxy statement for the 2024 annual meeting of stockholders.

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

The information required by Item 13 is hereby incorporated by reference to the information contained in our definitive proxy statement for the 2024 annual meeting of stockholders.

Item 14. Principal Accountant Fees and Services

The information required by Item 14 is hereby incorporated by reference to the information contained in our definitive proxy statement for the 2024 annual meeting of stockholders.

PART IV

Item 15. Exhibits and Financial Statement Schedules

The consolidated financial statements filed as part of this Annual Report on Form 10-K are listed in the Index to Consolidated Financial Statements. Certain schedules are omitted because they are not applicable, or not required, or because the required information is included in the consolidated financial statements or notes thereto. The Exhibits are listed in the Exhibit Index below.

EXHIBIT INDEX

Exhibit Number	Description
2.1	Asset Purchase Agreement, dated as of February 7, 2019, by and between Vimalan Biosciences, Inc. and the Registrant (incorporated by reference to Exhibit 2.1 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
2.2	Share Purchase Agreement, dated as of February 26, 2021, by and among the Registrant, Zomagen Biosciences Ltd. and certain of its Securityholders (incorporated by reference to Exhibit 2.2 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
2.3	Share Purchase Agreement, dated as of February 26, 2021, by and among the Registrant, Oppilan Pharma Ltd. and certain of its Securityholders (incorporated by reference to Exhibit 2.3 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended June 9, 2023 (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q, dated August 10, 2023.
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, dated December 12, 2022).
4.1	Amended and Restated Investors' Rights Agreement, dated as of September 9, 2021, by and among the Registrant and certain of its Stockholders (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
4.2	Specimen Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
4.3	Description of Common Stock (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K, dated March 24, 2022).
4.4	Form of Registration Rights Agreement, dated September 17, 2022, by and among the Registrant and the Purchasers thereto (incorporated by reference to Exhibit 10.2 on the Registrant's Current Report on Form 8-K filed on September 19, 2022).
10.1	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.2+	2019 Equity Incentive Plan, as amended, and forms of agreement thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.3+	2021 Equity Incentive Plan and forms of agreements thereunder (incorporated by reference to Exhibit 10.3 to the Registrant's Annual Report on Form 10-K, dated March 23, 2023).
10.4+	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.5+	Confirmatory Offer Letter, dated as of October 7, 2021, by and between Raju Mohan, Ph.D. and the Registrant (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.6+	Confirmatory Offer Letter, dated as of October 7, 2021, by and between Christopher Krueger, J.D., M.B.A. and the Registrant (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.7+	Confirmatory Offer Letter, dated as of October 7, 2021, by and between John Nuss, Ph.D. and the Registrant (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).

10.8+	Confirmatory Offer Letter, dated as of October 7, 2021, by and between Martin Auster, M.D. and the Registrant (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.9+	Executive Chairperson Offer Letter, dated as of May 14, 2021, by and between Sheila Gujrathi, M.D. and the Registrant (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.10	Lease, dated as of June 14, 2021, by and among Charlotta Partners, Inc., 9310 Towne Centre Drive Harrison-1, LLC and the Registrant (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.11	Master Services Agreement, dated as of January 17, 2019, by and between the Registrant and Bayside Pharma, LLC (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.12	Standard Multi-Tenant Office Lease, dated as of September 15, 2021, by and among Charlotta Partners, Inc., 9310 Towne Centre Drive Harrison-1, LLC and the Registrant (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1, File No. 333-259891).
10.13+	Executive Chairperson Services Agreement, dated as of May 14, 2021, by and between Sheila Gujrathi, M.D. and the Registrant (incorporated by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K, dated March 24, 2022).
10.14+	Employment Letter, dated May 5, 2022, by and between William J. Sandborn, M.D. and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, dated May 9, 2022).
10.15+	Executive Change in Control and Severance Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, dated May 9, 2022).
10.16+	Executive Incentive Compensation Plan (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K, dated March 23, 2023).
10.17	Lease, dated April 25, 2022, by and between Charlotta Partners, Inc. and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, dated August 15, 2022).
10.18	Form of Stock Purchase Agreement, dated September 17, 2022, by and among the Registrant and the Purchasers thereto (incorporated by reference to Exhibit 10.1 on the Registrant's Current Report on Form 8-K filed on September 19, 2022).
10.19	Open Market Sale Agreement[SM], dated as of December 20, 2022, by and between the Registrant and Jefferies LLC (incorporated by reference to Exhibit 1.2 on the Registrant's Registration Statement on Form S-3ASR, File No. 333-268909).
10.20+	Amended and Restated Outside Director Compensation Policy (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q, dated May 11, 2023).
10.21	Sublease Agreement, dated July 21, 2023, by and between the Registrant and Neurocrine Biosciences (incorporated by reference to Exhibit 10.1 on the Registrant's Current Report on Form 8-K, dated July 26, 2023).
10.22+*	Separation Agreement and Release, dated November 22, 2023, by and between the Registrant and William J. Sandborn
10.23+*	Consulting Agreement, dated November 20, 2023, by and between the Registrant and William J. Sandborn
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Annual Report on Form 10-K, dated March 23, 2023).
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1*	Powers of Attorney (contained in the signature page to this Annual Report on Form 10-K).

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**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of 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
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 Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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* Filed herewith.

** Furnished herewith.

+ Indicates management contract or compensatory plan.

Item 16. Form 10-K Summary

The Company has elected to not include a summary.

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 Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

VENTYX BIOSCIENCES, INC.

Date: February 27, 2024

By: /s/ Raju Mohan

Raju Mohan, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Date: February 27, 2024

By: /s/ Martin Auster

Martin Auster, M.D.
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Raju Mohan, Ph.D. and Martin Auster, M.D., as such individual's true and lawful attorney in fact and agent with full power of substitution, for such individual in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K (including post-effective amendments), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney in fact, proxy and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney in fact, proxy and agent, or the individual's substitute, may lawfully do or cause to be done by virtue hereof.

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

Name	Title	Date
/s/ Raju Mohan **Raju Mohan, Ph.D.**	Chief Executive Officer and Director *(Principal Executive Officer)*	February 27, 2024
/s/ Martin Auster **Martin Auster, M.D.**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 27, 2024
/s/ Sheila Gujrathi **Sheila Gujrathi, M.D.**	Executive Chairperson	February 27, 2024
/s/ Onaiza Cadoret-Manier **Onaiza Cadoret-Manier, M.B.A.**	Director	February 27, 2024
/s/ Allison J. Hulme **Allison J. Hulme, Ph.D.**	Director	February 27, 2024
/s/ Somasundaram Subramaniam **Somasundaram Subramaniam, M.B.A.**	Director	February 27, 2024
/s/ William White **William White, J.D., M.P.P.**	Director	February 27, 2024

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VENTYX BIOSCIENCES, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Ventyx Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ventyx Biosciences, Inc. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 27, 2024 expressed an unqualified opinion thereon.

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 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.

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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Estimated Clinical Trial Costs

Description of the Matter

The Company recorded research and development expenses of $175.8 million for the year ended December 31, 2023, which includes clinical trial costs. Research and development costs are expensed as incurred. As discussed in Note 2 to the consolidated financial statements, the Company estimates expenses incurred for clinical trial costs and services received and maintains a prepaid or accrual based on these costs. The Company estimates expenses incurred using assumptions about study and patient activities and the related expected expenses for those activities determined based on the contracted fees with service providers.

Auditing the Company's clinical trial costs is complex as the information necessary to estimate the accruals is accumulated from multiple sources. In addition, in certain circumstances, the determination of the nature and level of services that have been received during the reporting period requires judgment because the timing and pattern of vendor invoicing does not correspond to the level of services provided and there may be delays in invoicing from vendors.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the accumulation of data to estimate the clinical trial costs, which included controls over management's assessment of the assumptions and accuracy of data underlying the clinical trial costs estimate.

To test the Company's clinical trial costs, we performed audit procedures that included, among other procedures, obtaining supporting evidence of the activities performed for significant clinical trials and confirming expenses with the contract research organizations. We corroborated the status of significant clinical development costs through meetings with accounting and clinical project managers. We compared the costs for a sample of transactions against the related invoices and contracts and examined a sample of subsequent payments to evaluate the accuracy of the clinical trial costs and recalculated the ending prepaid or accrual for clinical trial costs.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2021.

San Diego, California
February 27, 2024

Ventyx Biosciences, Inc.
Consolidated Balance Sheets
(in thousands, except share amounts and par value data)

	December 31,	
	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 51,579	$ 64,819
Marketable securities	200,641	253,122
Prepaid expenses and other assets	12,125	12,747
Total current assets	264,345	330,688
Property and equipment, net	762	407
Operating lease right-of-use assets	11,509	1,537
Marketable securities	—	38,672
Restricted cash	975	—
Other long-term assets	102	96
Total assets	$ 277,693	$ 371,400
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,756	$ 6,433
Accrued expenses	15,508	9,514
Current portion of operating lease liabilities	1,001	412
Total current liabilities	22,265	16,359
Operating lease liabilities, net of current portion	11,505	1,146
Total liabilities	33,770	17,505
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Common stock, $0.0001 par value; 900,000,000 shares authorized at December 31, 2023 and December 31, 2022; 59,252,349 and 57,025,847 shares issued at December 31, 2023 and December 31, 2022, respectively; 59,239,113 and 56,980,845 shares outstanding at December 31, 2023 and December 31, 2022, respectively	6	6
Additional paid-in capital	663,154	581,237
Accumulated other comprehensive loss	(50)	(1,123)
Accumulated deficit	(419,187)	(226,225)
Total stockholders' equity	243,923	353,895
Total liabilities and stockholders' equity	$ 277,693	$ 371,400

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

Ventyx Biosciences, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year ended December 31,	
	2023	**2022**
Operating expenses:		
Research and development (includes related party amounts of $1,023 and $883, respectively)	$ 175,767	$ 87,738
General and administrative	32,227	25,398
Total operating expenses	207,994	113,136
Loss from operations	(207,994)	(113,136)
Other (income) expense:		
Interest income	(15,074)	(4,669)
Other (income) expense	42	(41)
Total other (income) expense	(15,032)	(4,710)
Net loss	$ (192,962)	$ (108,426)
Unrealized gain (loss) on marketable securities	1,121	(1,023)
Foreign currency translation	(48)	(42)
Comprehensive loss	$ (191,889)	$ (109,491)
Net loss per share attributable to common shareholders, basic and diluted	$ (3.30)	$ (2.07)
Shares used to compute basic and diluted net loss per share attributable to common shareholders	58,542,974	52,471,003

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

Ventyx Biosciences, Inc.
Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2022	56,980,845	$ 6	$ 581,237	$ (1,123)	$ (226,225)	$ 353,895
Issuance of common stock from at-the-market offering, net of commissions and offering expenses	1,176,470	—	48,408	—	—	48,408
Issuance of common stock upon exercise of stock options	837,922	—	4,671	—	—	4,671
Issuance of common stock upon vesting of restricted common stock	216,436	—	—	—	—	-
Shares issued under employee stock purchase plan	27,440	—	250	—	—	250
Stock-based compensation expense	—	—	28,588	—	—	28,588
Unrealized gain on marketable securities	—	—	—	1,121	—	1,121
Foreign currency translation	—	—	—	(48)	—	(48)
Net loss	—	—	—	—	(192,962)	(192,962)
Balance at December 31, 2023	59,239,113	$ 6	$ 663,154	$ (50)	$ (419,187)	$ 243,923

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2021	50,408,830	$ 5	$ 397,051	$ (58)	$ (117,799)	$ 279,199
Issuance of common stock from private placement, net of issuance costs	5,350,000	1	165,213	—	—	165,214
Issuance of common stock upon exercise of stock options	959,066	—	2,110	—	—	2,110
Issuance of common stock upon vesting of restricted common stock	241,792	—	—	—	—	—
Shares issued under employee stock purchase plan	21,157	—	267	—	—	267
Adjustment to offering expenses in the initial public offering	—	—	26	—	—	26
Stock-based compensation expense	—	—	16,570	—	—	16,570
Unrealized loss on marketable securities	—	—	—	(1,023)	—	(1,023)
Foreign currency translation	—	—	—	(42)	—	(42)
Net loss	—	—	—	—	(108,426)	(108,426)
Balance at December 31, 2022	56,980,845	$ 6	$ 581,237	$ (1,123)	$ (226,225)	$ 353,895

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

Ventyx Biosciences, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year ended December 31, 2023	2022
Cash flows from operating activities:		
Net loss	$ (192,962)	$ (108,426)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	158	123
Loss on impairment	285	—
Amortization of right-of-use assets - operating	783	347
Stock-based compensation	28,588	16,570
Accretion of marketable securities, net	(9,180)	(2,228)
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	616	(8,336)
Operating lease liabilities	(59)	(326)
Accounts payable	(745)	1,613
Accrued expenses	5,994	1,892
Net cash used in operating activities	(166,522)	(98,771)
Cash flows from investing activities:		
Purchases of marketable securities, available-for-sale	(272,271)	(347,236)
Proceeds from maturities of marketable securities, available-for-sale	373,725	272,580
Purchases of property and equipment	(514)	(275)
Net cash provided by (used in) investing activities	100,940	(74,931)
Cash flows from financing activities:		
Proceeds from issuance of common stock from at-the-market offering, net of commissions and offering expenses	48,408	—
Proceeds from issuance of common stock from private placement, net of offering costs	—	165,398
Proceeds from exercise of stock options	4,671	2,107
Proceeds from issuance of common stock under employee stock purchase plan	250	267
Net cash provided by financing activities	53,329	167,772
Effect of exchange rates on cash, cash equivalents and restricted cash	(12)	(42)
Net increase (decrease) in cash, cash equivalents and restricted cash	(12,265)	(5,972)
Cash, cash equivalents and restricted cash, beginning of year	64,819	70,791
Cash, cash equivalents and restricted cash, end of year	$ 52,554	$ 64,819
Supplemental disclosure for non-cash activities		
Unpaid private placement offering costs	$ —	$ 184
Purchases of property and equipment included in accounts payable and accrued expenses	$ 67	$ —

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

1. Organization and Business

Organization

Ventyx Biosciences, Inc. ("Ventyx" or "the Company") is a clinical-stage pharmaceutical company developing a pipeline of novel small molecule product candidates to address a range of inflammatory diseases with significant unmet medical need. The Company was incorporated in the State of Delaware in November 2018, with its principal operations in California. The Company leverages its drug discovery and development expertise to develop novel and differentiated therapeutics that target both the innate and adaptive immune system.

Liquidity and Capital Resources

The Company has experienced net losses since inception and, as of December 31, 2023, had an accumulated deficit of $419.2 million. From incorporation in November 2018 through December 31, 2023, the Company has devoted substantially all of its resources to organizing and staffing the Company, business planning, raising capital and identifying product candidates and conducting preclinical studies and clinical trials. Substantially all of the Company's operations have been funded through debt and equity financings. The Company does not have any products approved for sale and has not generated any revenue from product sales.

At December 31, 2023, the Company had cash, cash equivalents, and marketable securities of $252.2 million, excluding restricted cash of $1.0 million. As of the date of filing this Annual Report on Form 10-K, the Company has access to and control over all its cash, cash equivalents and marketable securities, notwithstanding the closure of Silicon Valley Bank. Since the Company's inception, the Company has incurred significant operating losses and, through the date of this report, has financed operations primarily through public offerings and private placements of our common stock, private placements of the Company's convertible preferred stock and convertible debt instruments.

Management expects to incur net losses for the foreseeable future. There can be no assurance that the Company will ever earn revenues or achieve profitability, or if achieved, that they will be sustained on a continuing basis. In addition, the preclinical manufacturing and clinical development activities, as well as the commercialization of the Company's products, if approved, will require significant additional financing. The Company may be unable to secure such financing when needed, or if available, such financings may be under terms that are unfavorable to the Company or the current stockholders. If the Company is unable to raise additional funds when needed, it may be required to delay, reduce the scope of, or eliminate development programs, which may adversely affect its business and operations.

Based on the Company's current business plan, management believes that existing cash, cash equivalents, and marketable securities will be sufficient to fund the Company's obligations for at least twelve months from the issuance of these consolidated financial statements. The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and settlement of liabilities in the normal course of business. The consolidated financial statements do not include any adjustments for the recovery and classification of assets or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements were prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and with the rules and regulations of the United States ("U.S.") Securities and Exchange Commission ("SEC"). The presentation of the Company's consolidated financial statements for the periods presented reflect the financial results of Ventyx Biosciences, Inc. on a consolidated basis. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the Company's consolidated financial statements and accompanying notes. On an

ongoing basis, the Company evaluates its estimates and judgments, which are based on historical and anticipated results and trends and on various other assumptions that management believes to be reasonable under the circumstances. Significant estimates include, but are not limited to, estimates related to prepaid and accrued clinical trial and research and development costs, the measurement of the fair value of stock-based awards, available-for-sale marketable securities, the measurement of operating lease right-of-use assets and operating lease liabilities, and the evaluation of long-lived assets for impairment. By their nature, estimates are subject to an inherent degree of uncertainty and, as such, actual results may differ from management's estimates.

Risks and Uncertainties

Economic uncertainty in various global markets, including the U.S. and Europe, caused by political instability and conflict, such as the military conflicts in Ukraine and the Middle East, and economic challenges caused by the COVID-19 pandemic, have led to market disruptions, including significant volatility in commodity prices, credit and capital market instability and supply chain interruptions, which have caused volatile changes to inflation globally. The Company's business, financial condition and results of operations could be materially and adversely affected by further negative impact on the global economy and capital markets resulting from these or future global economic conditions, particularly if such conditions are prolonged or worsen.

Although, to date, the Company has not been materially impacted by these global economic and geopolitical conditions, it is impossible to predict the extent to which operations will be impacted in the short and long term, or the ways in which such instability could impact business and results of operations. The extent and duration of these market disruptions, whether as a result of military conflicts and effects of sanctions, geopolitical tensions, volatile changes to inflation or otherwise, are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this report.

Segments

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker ("CODM"), the Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business as one operating segment.

Cash and Cash Equivalents

The Company considers all short-term, highly liquid investments that are readily convertible to cash with original maturities of three months or less at acquisition date to be cash equivalents. Cash equivalents are stated at fair value and have consisted of money market accounts, corporate debt securities and commercial paper.

Investments in Marketable Securities, Available-for-Sale

The Company maintains a portfolio of investments which have included U.S. Treasury securities, U.S. government agency securities, corporate debt securities, commercial paper and asset-backed securities ("ABS"). The Company's investments in marketable securities are available-for-sale securities and the marketable securities are reported at fair value. Investments in marketable securities with contractual maturities less than 12 months at the balance sheet date are considered short-term investments. Those investments in marketable securities with contractual maturities of 12 months or greater at the balance sheet date are considered long-term investments. Unrealized gains and losses are included in accumulated other comprehensive loss, net of tax. The cost of securities sold is determined on a specific identification basis, and realized gains and losses, if any, are included in other (income) expense within the consolidated statements of operations and comprehensive loss.

The Company regularly reviews its investment portfolio to determine if any security is impaired, which would require the Company to record an impairment charge in the period that any such determination is made. Calculating an impairment charge requires judgment. In making this judgment, the Company evaluates, among other items, the time frame and extent to which the fair market value of a security is less than its amortized cost and the Company's intent and ability to sell, or whether the Company will more likely than not be required to sell the security before recovery of its amortized cost basis.

Property and Equipment

The Company records property and equipment, which consists of laboratory equipment, furniture and fixtures, computer hardware and software and internal-use software, at cost less accumulated depreciation. Property and equipment is depreciated using the straight-line method over the estimated useful lives which ranges from three to seven years.

The Company follows Accounting Standards Codification ("ASC") 350-40, *Intangibles-Goodwill and Other, Internal-Use Software*, ("ASC 350-40") to account for development costs incurred for the costs of computer software obtained for internal use. ASC 350-40 requires such costs to be capitalized once certain criteria are met. Capitalized internal-use software costs are primarily comprised of direct labor, related expenses and initial software licenses. ASC 350-40 includes specific guidance on costs not to be capitalized, such as overhead, general and administrative and training costs. Internal-use software includes software utilized for cloud-based solutions as well as software for internal systems and tools. Costs are capitalized once the project is defined, funding is committed and it is confirmed the software will be used for its intended purpose. Capitalization of these costs concludes once the project is substantially complete and the software is ready for its intended purpose. Post-configuration training and maintenance costs are expensed as incurred. During the years ended December 31, 2023 and 2022, the Company capitalized $0.3 million and $0.2 million of internal-use software costs, respectively.

The Company evaluates its property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

Restricted Cash

Under the terms of the Company's Sublease Agreement (the "Sublease") executed in July 2023 with Neurocrine Biosciences, Inc. ("Neurocrine") for office space in San Diego, California, Bank of America issued on the Company's behalf an irrevocable standby letter of credit in the amount of $0.5 million. Additionally, in August 2023, the Company opened a corporate credit card account with Bank of America requiring a secured cash deposit of $0.5 million. Both the letter of credit and secured credit card are secured by deposits totaling $1.0 million with the same bank. The Company classified these deposits as restricted cash in the consolidated balance sheet as of December 31, 2023.

A reconciliation of the cash, cash equivalents and restricted cash reported in our consolidated balance sheets that sum to the total of the amounts shown in the consolidated statements of cash flows is as follows (in thousands):

	December 31,	
	2023	**2022**
Cash and cash equivalents	$ 51,579	$ 64,819
Restricted cash	975	—
Total cash, cash equivalents and restricted cash	$ 52,554	$ 64,819

Impairment of Long-Lived Assets

The Company reviews long-lived assets, primarily comprised of property, equipment and operating lease right-of-use ("ROU") assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of the asset or asset group to future undiscounted cash flows expected to be generated by the asset or asset group. If the asset or asset group is determined to be impaired, the impairment recognized is measured by the amount by which the carrying value of the asset or asset group exceeds the projected discounted future net cash flows arising from the asset or asset group.

As a result of the Company entering into the Sublease in July 2023 with Neurocrine for office space in San Diego, California which became the Company's headquarters in August 2023, the Company determined impairment testing triggers had occurred for the Encinitas, California ROU asset and the associated furniture and fixtures (collectively, the "Encinitas Asset Group") as of July 21, 2023. Accordingly, the Company analyzed undiscounted cash flows for the Encinitas Asset Group. Based on the undiscounted cash flow analysis, the Company determined that the estimated net carrying value of the Encinitas Asset Group exceeded undiscounted cash flows and therefore, the Encinitas Asset Group was impaired and recorded a loss on impairment of $0.3 million. See Note 7, *Leases*, in the notes to the consolidated financial statements for further discussion.

Assumptions and estimates used to determine cash flows in the evaluation of impairment and the fair values used to determine the impairment are subject to a degree of judgment and complexity. Any future changes to the assumptions and estimates resulting from changes in actual results or market conditions from those anticipated may affect the carrying value of long-lived assets and could result in additional impairment charges, and such changes could be material.

Concentration of Credit Risk

The Company's financial instruments that are exposed to concentrations of credit risk consist primarily of cash and cash equivalents, available-for-sale marketable securities and restricted cash. The Company maintains deposits in government insured financial institutions in excess of government insured limits. The Company invests its cash balances in financial institutions that it believes have high credit quality, has not experienced any losses on such accounts and does not believe it is exposed to significant credit risk. The Company purchases its available-for-sale marketable securities with financial institutions which management believes have high credit ratings. The Company performs periodic evaluations of the credit standing of the financial institutions for which it has marketable securities with. Additionally, the Company has adopted investment guidelines that limit the amounts the Company may invest in any one type of investment and requires all investments held by the Company to be highly rated, thereby reducing credit risk exposure.

Deferred Offering Costs

The Company defers offering costs consisting of accounting and legal fees directly attributable to the issuance of equity and debt securities until the successful completion of such issuances, at which time they are reclassified to additional paid-in capital as a reduction against the proceeds received.

Fair Value of Financial Instruments

The Company follows Accounting Standards Codification ("ASC") 820-10, *Fair Value Measurements and Disclosures* ("ASC 820-10"), issued by the Financial Accounting Standards Board ("FASB") with respect to fair value reporting for financial and non-financial assets and liabilities. The carrying amounts of the Company's current financial assets and current financial liabilities are considered to be representative of their respective fair values because of the short-term nature of those instruments. Financial assets measured at fair value on a recurring basis include cash equivalents and marketable securities.

Certain non-financial assets are measured at fair value on a nonrecurring basis, generally as a result of the remeasurement of assets resulting in impairment charges. The Company utilizes Level 3 inputs in the determination of the initial fair value using certain assumptions. Non-financial assets, such as ROU assets and property and equipment, are subsequently measured at fair value when there is an indicator of impairment and recorded at fair value when impairment is recognized. None of the Company's non-financial liabilities are recorded at fair value on a nonrecurring basis.

Research and Development Expenses

The Company's research and development costs consist primarily of salaries, payroll taxes, employee benefits and stock-based compensation charges for those individuals involved in ongoing research and development efforts; as well as fees paid to consultants, third party research organizations, laboratory supplies and development compound materials. All research and development costs are charged to expense as incurred.

Clinical Trial Expenses

The Company makes payments in connection with its clinical trials under contracts with contract research organizations that support conducting and managing clinical trials. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Generally, these agreements set forth the scope of work to be performed at a fixed fee, unit price or on a time and materials basis. A portion of the Company's obligation to make payments under these contracts depends on factors such as the successful enrollment or treatment of patients or the completion of other clinical trial milestones.

Expenses related to clinical trials are accrued based on estimates and/or representations from service providers regarding work performed, including actual level of patient enrollment, completion of patient studies and progress of the clinical trials. Other incidental costs related to patient enrollment or treatment are accrued when reasonably certain. If the amounts the Company is obligated to pay under clinical trial agreements are modified (for instance, as a result of changes in the clinical trial protocol or scope of work to be performed), the Company adjusts the accruals accordingly. Revisions to the contractual payment obligations are charged to expense in the period in which the facts that give rise to the revision become reasonably certain.

General and Administrative Expenses

General and administrative expenses are related to finance, human resources, legal and the Company's other administrative activities. These expenses consist primarily of personnel costs, including stock-based compensation expenses, outside services, legal expenses,

management fees and other general and administrative costs. Additionally, these expenses consist of costs related to filing and pursuing patent applications. These patent costs are expensed as incurred, as recoverability of such expenditures is uncertain.

Income Taxes

The Company follows FASB ASC 740, *Income Taxes* ("ASC 740"), in reporting deferred income taxes. ASC 740 requires a company to recognize deferred tax assets and liabilities for expected future income tax consequences of events that have been recognized in the Company's consolidated financial statements. Under this method, deferred tax assets and liabilities are determined based on temporary differences between financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates in the years in which the temporary differences are expected to reverse. Valuation allowances are provided if, based on 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 pursuant to ASC 740, which prescribes a recognition threshold and measurement process for financial statement recognition of uncertain tax positions taken or expected to be taken in a tax return. If the tax positions meet this threshold, the benefit to be recognized is measured as the tax benefit having the highest likelihood of being realized upon ultimate settlement with the taxing authority. The Company recognizes interest accrued related to unrecognized tax benefits and penalties in the provision for income taxes.

Stock-Based Compensation

The Company measures the compensation expense of stock-based awards granted to employees and directors using the grant date fair value of the award. The Company has issued stock options, restricted stock awards ("RSA") and restricted stock units ("RSU") with service-based vesting conditions. The Company measures the compensation expense of stock-based awards granted to employees and nonemployees using the grant date fair value of the award. The Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period for employees and over the period during which services are rendered by nonemployees. Forfeitures are recognized in the period in which they occur.

The Company estimates the fair value of stock options using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (a) the risk-free interest rate, (b) the expected volatility of the Company's stock, (c) the expected term of the award, and (d) the expected dividend yield. Due to the lack of an adequate history of a public market for the trading of the Company's common stock, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, the Company has selected companies with comparable characteristics, including enterprise value, risk profiles, and position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company has estimated the expected life of its employee stock options using the "simplified" method, whereby the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the yields of zero-coupon U.S. treasury securities.

The fair value of RSAs and RSUs is measured using the closing price of the Company's common stock on the date of grant.

Restructuring Costs

The Company defines restructuring costs as expenses directly associated with restructuring activities. Such costs include severance and related tax and benefit expenses from workforce reductions. For one-time termination benefits, the cost is recorded when the term of the one-time benefits are communicated to the impacted employees and the employees are not required to render service beyond a minimum retention period. If employees are required to render service beyond a minimum retention period, the liability for the termination benefits is measured initially at the communication date based on the fair value of the liability as of the termination date, and is recognized ratably over the future service period.

Net Loss Per Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed using the sum of the weighted average number of common shares outstanding during the period, plus the weighted average number of potential shares of common stock from the assumed exercise of stock options, the assumed vesting of restricted stock awards and restricted stock units and the number of shares purchasable under the 2021 Employee Stock Purchase Plan ("2021 ESPP"), if dilutive. Since the Company was in a net loss position, basic and diluted net loss per share was the same for each of the periods presented.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss is comprised of net loss, foreign currency translation adjustments and unrealized gains (losses) on marketable securities.

Recent Accounting Pronouncements

Recently Issued Accounting Pronouncements Not Yet Adopted

In August 2020, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in Entity's Own Equity* ("ASU 2020-06"), which, among other things, provides guidance on how to account for contracts on an entity's own equity. This ASU simplifies the accounting for certain financial instruments with characteristics of liabilities and equity. Specifically, the ASU eliminated the need for the Company to assess whether a contract on the entity's own equity (1) permits settlement in unregistered shares, (2) whether counterparty rights rank higher than shareholder's rights, and (3) whether collateral is required. In addition, this ASU requires incremental disclosure related to contracts on the entity's own equity and clarifies the treatment of certain financial instruments accounted for under this ASU on earnings per share. This ASU may be applied on a full retrospective or modified retrospective basis. The amendments within this ASU are effective for the Company's fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption of the ASU is permitted to fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial statements and related disclosures.

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*. The ASU expands public entities' segment disclosures by requiring disclosure of significant segment expenses that are regularly reviewed by the CODM and included within each reported measure of segment profit or loss, an amount and description of its composition for other segment items, and interim disclosures of a reportable segment's profit or loss and assets. The ASU also allows, in addition to the measure that is most consistent with U.S. GAAP, the disclosure of additional measures of segment profit or loss that are used by the CODM in assessing segment performance and deciding how to allocate resources. All disclosure requirements under ASU 2023-07 are also required for public entities with a single reportable segment. The ASU is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, on a retrospective basis, with early adoption permitted. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial statements and related disclosures.

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*. The update requires a public business entity to disclose, on an annual basis, a tabular rate reconciliation using both percentages and currency amounts, broken out into specified categories with certain reconciling items further broken out by nature and jurisdiction to the extent those items exceed a specified threshold. In addition, all entities are required to disclose income taxes paid, net of refunds received disaggregated by federal, state/local, and foreign and by jurisdiction if the amount is at least 5% of total income tax payments, net of refunds received. Adoption of the ASU allows for either the prospective or retrospective application of the amendment and is effective for annual periods beginning after December 15, 2024, with early adoption permitted. The Company has not yet completed its assessment of the impact of ASU 2023-09 on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses: Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13") which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses on certain types of financial instruments, including trade receivables and available-for-sale debt securities. The Company adopted this standard on January 1, 2023 and as the Company does not have material trade or financing receivables or held to maturity debt securities, and as management does not expect to incur credit losses on available-for-sale marketable debt securities held by the Company, the adoption of this standard did not have a material impact to the consolidated financial statements at the adoption date.

3. Fair Value Measurements

Fair value is defined as the exchange price that would be received to sell an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at 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 fair value hierarchy is as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Inputs, other than the quoted prices included in Level 1, that are either directly or indirectly observable.

Level 3: Unobservable inputs in which there is little or no market activity, which require the reporting entity to develop its own assumptions.

The following tables present information about the fair value measurements of the Company's financial assets and liabilities which are measured at fair value on a recurring basis, and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	December 31, 2023			
	Level 1	**Level 2**	**Level 3**	**Total**
Assets:				
Cash equivalents				
Money market fund	$ 40,241	$ —	$ —	$ 40,241
Commercial paper	—	7,468	—	7,468
Total cash equivalents	40,241	7,468	—	47,709
Marketable securities				
U.S. government agency securities	—	67,208	—	67,208
Commercial paper	—	118,465	—	118,465
Asset backed securities	—	14,968	—	14,968
Total marketable securities	—	200,641	—	200,641
Total assets	$ 40,241	$ 208,109	$ —	$ 248,350

	December 31, 2022			
	Level 1	**Level 2**	**Level 3**	**Total**
Assets:				
Cash equivalents				
Money market fund	$ 22,721	$ —	$ —	$ 22,721
Total cash equivalents	22,721	—	—	22,721
Marketable securities				
U.S. Treasury securities	39,567	—	—	39,567
U.S. government agency securities	—	74,979	—	74,979
Corporate debt securities	—	2,990	—	2,990
Commercial paper	—	171,866	—	171,866
Asset backed securities	—	2,392	—	2,392
Total marketable securities	39,567	252,227	—	291,794
Total assets	$ 62,288	$ 252,227	$ —	$ 314,515

In determining the fair value of its Level 2 investments, the Company relied on the most recent observable inputs for similar instruments in active markets or quoted prices for identical or similar instruments in markets that are not active or are directly or indirectly observable. These quoted prices were obtained by the Company with the assistance of a third-party pricing service based on available trade, bid or other observable market data for identical or similar securities. During the years ended December 31, 2023, 2022, there were no transfers between Level 1, Level 2 and Level 3.

As of December 31, 2023 and 2022, the fair value of the Company's available-for-sale marketable securities by type of security was as follows (in thousands):

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Marketable securities:				
U.S. government agency securities	$ 67,310	$ —	$ (102)	$ 67,208
Commercial paper	118,323	143	(1)	118,465
Asset backed securities	14,979	2	(13)	14,968
Total marketable securities	$ 200,612	$ 145	$ (116)	$ 200,641

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Marketable securities:				
U.S. Treasury securities	$ 39,989	$ —	$ (422)	$ 39,567
U.S. government agency securities	75,337	—	(358)	74,979
Corporate debt securities	3,005	—	(15)	2,990
Commercial paper	172,162	20	(316)	171,866
Asset backed securities	2,393	—	(1)	2,392
Total marketable securities	$ 292,886	$ 20	$ (1,112)	$ 291,794

All of the Company's marketable securities as of December 31, 2023 have maturity dates of less than one year.

The Company reviews its marketable securities at each reporting date to determine if any security is other-than-temporarily impaired, which would require the Company to record an impairment charge in that respective period. In making this judgment, the Company considers the intent and ability to retain the investment for a period of time sufficient to allow for any anticipated recovery in market value and the duration and extent that the market value has been less than cost.

As of December 31, 2023, 10 available-for-sale marketable securities were in an unrealized loss position. Of the 10 available-for-sale marketable securities in an unrealized loss position, 8 had been in an unrealized loss position for less than 12 months and 2 had been in an unrealized loss position for greater than 12 months. As of December 31, 2022, 37 available-for-sale marketable securities were in an unrealized loss position. Of the 37 available-for-sale marketable securities in an unrealized loss position, 32 had been in an unrealized loss position for less than 12 months and 5 had been in an unrealized loss position for greater than 12 months.

The Company evaluated the securities individually for impairment and considered factors such as the severity of the impairment, changes in underlying credit ratings, forecasted recovery, the Company's intent to sell or the likelihood that the Company would be required to sell the security before its anticipated recovery in market value and the probability that the scheduled cash payments will continue to be made. Based on the Company's review of these marketable securities, the Company believes none of the unrealized losses are the result of a credit loss as of December 31, 2023 and 2022 because the Company does not intend to sell these securities prior to maturity and it is not more-likely-than-not that the Company will be required to sell these securities before the recovery of their amortized cost basis. As such, the Company did not record an allowance for credit losses as of December 31, 2023 and 2022. The decline in market value in the Company's marketable securities was primarily attributable to an increase in interest rates during the years ended December 31, 2023 and 2022.

Accrued interest receivable on available-for-sale marketable securities, included in prepaid expenses and other assets on the Company's consolidated balance sheets, was $0.8 million and $0.9 million at December 31, 2023 and 2022, respectively.

Nonrecurring Fair Value Measurements

During the year ended December 31, 2023, the Company measured the Encinitas Asset Group at fair value, which resulted in impairment charges. The fair value of the Encinitas Asset Group was determined using a discounted cash flow ("DCF") model, which estimated the

net present value of future net cash flows that a market participant would pay to use the Encinitas Asset Group for the remaining lease term. The key inputs to the DCF model included future projections of cash rental payments and a discount rate.

4. Consolidated Balance Sheet Details

Property and Equipment, net

Property and equipment, net as of December 31, 2023 and 2022 consisted of the following (in thousands):

	December 31,	
	2023	**2022**
Internal-use software	$ 491	$ 188
Laboratory equipment	178	142
Furniture and fixtures	137	104
Computer hardware and software	58	68
Construction in progress	157	—
Property and equipment, gross	1,021	502
Less: accumulated depreciation	(259)	(95)
Property and equipment, net	$ 762	$ 407

During the years ended December 31, 2023 and 2022, depreciation expense was approximately $0.2 million and $0.1 million, respectively.

Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2023	**2022**
Accrued research and development costs	$ 1,868	$ 2,450
Accrued clinical trial costs	4,831	1,235
Accrued payroll liabilities	7,742	4,208
Other accrued liabilities	984	1,557
Accrued related party liabilities	83	64
Total accrued expenses	$ 15,508	$ 9,514

On December 5, 2023, the Company committed to and implemented a reduction in force ("RIF") and incurred one-time termination benefits associated with severance payment obligations and continued healthcare benefits for employees terminated under the RIF. During the year ended December 31, 2023, the Company recorded a charge of $2.2 million associated with the RIF of which $1.7 million was recorded in research and development expenses and $0.5 million was included in general and administrative expenses. As of December 31, 2023, $2.2 million is included in accrued payroll liabilities.

5. Commitments and Contingencies

Litigation

In the ordinary course of its business, the Company may be involved in various legal proceedings involving contractual and employment relationships, patent or other intellectual property rights, and a variety of other matters. The Company is not aware of any pending legal proceedings that would reasonably be expected to have a material impact on the Company's financial position or results of operations.

6. Stockholders' Equity

ATM Sales Agreement

In December 2022, the Company entered into Open Market Sales Agreement℠ ("Sales Agreement") with Jefferies LLC ("Jefferies"), as sales agent, pursuant to which the Company may offer and sell in an at-the-market offering, from time to time through Jefferies, shares of common stock providing for aggregate sales proceeds of up to $150.0 million. The Company has no obligation to sell any shares under the Sales Agreement, and could at any time suspend solicitations and offers under the Sales Agreement.

In February 2023, the Company issued and sold 1,176,470 shares of common stock through the Sales Agreement. The common stock had an average purchase price of $42.50 per share for aggregate gross proceeds of $50.0 million. The Company received approximately $48.4 million in net proceeds after deducting commissions and offering expenses payable by the Company.

September 2022 Private Placement

In September 2022, the Company issued and sold 5,350,000 shares of its common stock in a private placement at an offering price of $33.00 per share for aggregate gross proceeds of approximately $176.6 million. The Company received $165.2 million in net proceeds after deducting fees to the placement agents and offering expenses payable by the Company.

Common Stock

The Company is authorized to issue up to 900,000,000 shares of common stock having a par value of $0.0001 par value as of December 31, 2023 and 2022. Holders of outstanding shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders. Subject to the rights of the holders of any class of the Company's capital stock having any preference or priority over common stock, the holders of common stock are entitled to receive dividends that are declared by the Company's board of directors out of legally available funds.

Common stock reserved for future issuance is as follows (in common stock equivalents shares) as of December 31, 2023:

	December 31, 2023
Issued and outstanding:	
Stock options	10,338,724
Restricted stock awards	13,236
Restricted stock units	530,726
Authorized for future stock award grants:	
2021 Equity Incentive Plan	317,001
2021 Employee Stock Purchase Plan	1,031,661
Total	12,231,348

7. Leases

In July 2023, the Company entered into a Sublease with Neurocrine for office space in San Diego, California which became the Company's headquarters in August 2023. Under the terms of the Sublease, the Company leased the second floor of the building, including certain furniture and fixtures, located at 12790 El Camino Real in San Diego, California consisting of approximately 35,016 rentable square feet of office space. The term of this non-cancellable lease commenced on July 21, 2023, and will end on July 31, 2031. The Company is subleasing the premises for $1.0 million in the first year with 3% annual increases in each subsequent year. The Sublease included rent abatement for the second through the seventh full calendar months of the lease term. In lieu of a cash security deposit under the Sublease, Bank of America issued on the Company's behalf an irrevocable standby letter of credit in the amount of $0.5 million. The letter of credit is secured by a deposit of $0.5 million with the same bank. In applying ASC 842, the Company elected the practical expedient to not separate non-lease components from lease components and concluded the Sublease should be classified as an operating lease. As the Sublease did not provide an implicit rate, the Company used its incremental borrowing rate available at commencement date in determining the present value of lease payments. The Company recognized an operating lease liability of $11.0 million and a corresponding operating lease right-of-use asset of approximately $11.0 million during the year ended December 31, 2023.

In February 2021, the Company assumed an operating lease in Encinitas, California for its office facilities, and in June 2021 the Company signed an amendment to add an additional term and additional suites in the office building in Encinitas, California. This non-cancellable lease expires on June 30, 2026. In September 2021, the Company executed an operating lease which adds existing office space in its existing building in Encinitas, California. The non-cancellable lease also expires on June 30, 2026.

In May 2022, the Company entered into a lease agreement to add office space to its existing lease in Encinitas, California. The non-cancellable lease commenced on June 1, 2022 and expires on June 30, 2026. The office building leases do not contain renewal options.

In March 2021, the Company signed a three-year operating lease for a multi-function ventilated research laboratory and office space in Ghent, Belgium. The non-cancellable lease expires on June 30, 2024. This laboratory and office space lease includes two, two-year renewal options.

As noted in Note 2, *Summary of Significant Accounting Policies*, the Company tests ROU assets when impairment indicators are present. The Company determined impairment triggers had occurred for the Encinitas Asset Group when the Sublease was executed and the Company moved its headquarters to the office space in San Diego, California. Therefore, the Company performed an undiscounted cash flow analysis for the Encinitas Asset Group as of July 21, 2023. Based on the undiscounted cash flow analysis, the Company determined the Encinitas Asset Group had a net carrying value that exceeded its estimated undiscounted future cash flows and the fair value for the Encinitas Asset Group. The fair value of the Encinitas Asset Group measured on a non-recurring basis, which is classified as Level 3 in the fair value hierarchy, was determined based on estimates of future discounted cash flows. The estimated fair value was compared to the net carrying value and as a result, the Encinitas Asset Group held and used with a carrying amount of $1.4 million was determined to have a fair value of $1.1 million, resulting in an impairment charge of $0.3 million, of which an immaterial amount was associated with the furniture and fixtures included in the Encinitas Asset Group. During the year ended December 31, 2023, $0.2 million of the impairment charge was recorded in research and development expenses and $0.1 million of the impairment charge was recorded in general and administrative expenses within the consolidated statements of operations and comprehensive loss.

The Company's leases have remaining terms ranging between one year to eight years. The leases contain various termination options. The Company leases do not contain any residual value guarantees or material restrictive covenants.

The weighted average remaining lease term and discount rate for the Company's operating leases were approximately 7.1 years and 10.0%, respectively, at December 31, 2023.

During the years ended December 31, 2023 and 2022, the Company recognized operating lease costs of $1.5 million and $0.5 million, respectively, and an immaterial amount of variable lease costs in both periods. In addition, the Company made cash payments of $0.7 million and $0.5 million for operating leases during the years ended December 31, 2023 and 2022, respectively, which are included in cash flows from operating activities in the consolidated statements of cash flows.

Supplemental cash flow information related to operating leases for the years ended December 31, 2023 and 2022 is as follows (in thousands):

	Year ended December 31,	
	2023	2022
Noncash activity:		
Right-of-use assets obtained in exchange for operating lease liabilities	$ 11,007	$ 508
Right-of-use assets obtained in exchange for operating lease liabilities in connection with adoption of new lease standard	$ —	$ 1,384

The Company's right-of-use assets and lease liabilities were as follows at December 31, 2023 and 2022 (in thousands):

	December 31,	
	2023	2022
Assets:		
Operating lease right-of-use assets	$ 11,509	$ 1,537
Liabilities:		
Current portion of operating lease liabilities	1,001	412
Operating lease liabilities, net of current portion	11,505	1,146
Total lease liabilities	$ 12,506	$ 1,558

Future minimum payments under non-cancellable leases as of December 31, 2023 were as follows (in thousands):

Years ending December 31,	
2024	$ 2,198
2025	2,575
2026	2,390
2027	2,199
2028	2,265
Thereafter	6,162
Total future minimum lease payments	17,789
Less: imputed interest	(5,283)
Present value of lease liabilities	12,506
Less: lease liabilities, current	(1,001)
Lease liabilities, net of current portion	$ 11,505

8. Stock-Based Compensation

Equity Incentive Plans

In February 2019, the Company adopted its 2019 Equity Incentive Plan (the "2019 Plan"). In October 2021, the 2019 Plan was terminated as to new awards upon the adoption of the 2021 Equity Incentive Plan (the "2021 Plan"), which became effective on October 19, 2021. The 2021 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and performance awards to employees, directors or consultants of the Company.

The number of common shares available for issuance under the 2021 Plan is 5,612,000 shares of common stock plus any common shares subject to stock options, restricted stock units or similar awards granted under the 2019 Plan that expire, are forfeited or otherwise terminate without having been exercised in full, are tendered to or withheld by the Company for payment of an exercise price or for tax withholding obligations or are forfeited to or repurchased by the Company due to failure to vest, with the maximum number of common shares to be added to the 2021 Plan equal to 4,978,561 common shares. Additionally, shares available for issuance under the 2021 Plan increase on the first day of each fiscal year, beginning with the Company's 2023 fiscal year, equal to the lesser of 5,102,000 common shares, 5% of the outstanding common shares on the last day of the immediately preceding fiscal year, or such number of common shares determined by the board of directors. On January 1, 2024 and 2023, the number of shares of common stock that may be issued under the 2021 Plan was automatically increased by 2,962,617 and 2,851,292 shares, respectively.

Options granted under the 2019 Plan and 2021 Plan (collectively, the "Plans") generally vest over a period of between one and four years and expire ten years from grant date. As of December 31, 2023 and 2022, the Company had 9,018,173 and 6,161,504 shares, respectively, authorized for issuance under the Plans, and 317,001 and 1,195,138 shares, respectively, remained available for grant.

Total share-based compensation expense was comprised of the following (in thousands):

	Year ended December 31,	
	2023	2022
Research and development	$ 14,590	$ 6,619
General and administrative	13,998	9,951
Total stock-based compensation expense	$ 28,588	$ 16,570

Stock-based compensation expense by type of share-based award (in thousands):

	Year ended December 31,	
	2023	2022
Stock options	$ 24,241	$ 13,642
Restricted stock awards	109	111
Restricted stock units	4,030	2,635
Employee Stock Purchase Plan	208	182
Total stock-based compensation expense	$ 28,588	$ 16,570

Stock Options

The following table summarizes stock option activity for the year ended December 31, 2023:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2022	7,592,856	$ 11.82	8.74	$ 159,929
Granted	4,772,252	20.66		
Exercised	(837,922)	5.57		
Forfeited and cancelled	(1,188,462)	28.97		
Outstanding as of December 31, 2023	10,338,724	$ 14.42	8.24	$ 1,737
Options vested and expected to vest as of December 31, 2023	10,338,724	$ 14.42	8.24	$ 1,737
Options exercisable as of December 31, 2023	4,091,946	$ 11.99	7.28	$ 1,061

The weighted average grant date fair value of stock options granted during the years ended December 31, 2023 and 2022 was $13.44 and $11.36 per share, respectively. The intrinsic value of a stock option is the difference between the market price of the common stock at measurement date and the exercise price of the option. The total intrinsic value of stock options exercised during the year ended December 31, 2023 and 2022 was $23.8 million and $17.7 million, respectively.

The fair value of each option award is estimated on the date of grant using the Black-Scholes model. The following assumptions were used in the Black-Scholes option pricing model to estimate the fair value of stock options granted to employees under the Company's Plans during the periods presented:

	Year ended December 31,	
	2023	2022
Risk-free interest rate	3.4% - 5.4%	0.9% - 4.4%
Expected volatility	67.5% - 100.4%	67.9% - 75.0%
Expected term (in years)	0.3 - 10.0	0.3 - 10.0
Expected dividend yield	—	—

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero coupon U.S. Treasury bonds with maturities similar to the expected term of the award being valued.

Expected volatility. Given the Company's limited historical stock price volatility data, the expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biotechnology industry. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determined the expected life assumption using the simplified method for employees, which is an average of the contractual term of the option and its vesting period. The expected term for nonemployee options is generally the contractual term.

Expected dividend yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends and, therefore, used an expected dividend yield of zero.

During the year ended December 31, 2023, the Company recorded a net decrease to stock-based compensation expense of approximately $1.4 million pertaining to the net impact of the modification of stock options in connection with the termination of five employees and the related reversal of estimated expenses associated with unvested awards upon the modification date. During the year ended December 31, 2022, the Company recorded incremental stock-based compensation expense of approximately $0.3 million pertaining to the modification of stock options in connection with the termination of two employees. The modifications provided for an acceleration of unvested options, resulting in additional compensation expense that was immediately recognized. As of December 31, 2023, unrecognized stock-based compensation was $54.4 million which is expected to be recognized over the weighted average period of 3.0 years.

Restricted Stock Awards

The Company grants restricted stock awards pursuant to the Plans and satisfies such grants through the issuance of new shares. Restricted stock awards generally vest over a period of 3 years. Upon the termination of service of a restricted stockholder, the Company has the option to repurchase any unvested shares and based on this, restricted stock awards are not included in outstanding common stock until fully vested. During the years ended December 31, 2023 and 2022, the Company did not repurchase any unvested shares, respectively.

The following table summarizes restricted stock award activity for the year ended December 31, 2023:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
Unvested balance as of December 31, 2022	45,002	$ 3.45
Vested	(31,766)	3.45
Unvested balance as of December 31, 2023	13,236	$ 3.45

The Company records a liability for unvested restricted stock awards subject to repurchase and reduces the liability as the underlying shares vest. The liability was immaterial as of December 31, 2023 and 2022. The total fair value of restricted stock awards vested during the years ended December 31, 2023 and 2022 was immaterial. As of December 31, 2023, there was an immaterial amount of unrecognized stock-based compensation cost pertaining to restricted stock awards that will be recognized over a weighted average period of 0.3 years.

Restricted Stock Units

The Company grants restricted stock units pursuant to the Plans and satisfies such grants through the issuance of new shares as they vest. Restricted stock units generally vest over a period of 4 years. The following table summarizes restricted stock unit activity for the year ended December 31, 2023:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
Balance as of December 31, 2022	569,757	$ 15.86
Granted	203,511	32.83
Vested	(184,670)	15.61
Forfeited and cancelled	(57,872)	28.20
Unvested balance as of December 31, 2023	530,726	$ 21.11

As of December 31, 2023, $9.3 million of unrecognized stock-based compensation cost pertaining to restricted stock units that will be recognized over a weighted average period of 2.4 years.

Employee Stock Purchase Plan

In October 2021, the board of directors and stockholders approved the 2021 Employee Stock Purchase Plan which became effective on October 19, 2021. The maximum number of shares of common stock that will be made available for sale under the 2021 ESPP is equal to 510,000 shares of common stock. In addition, the number of shares of common stock available for issuance under the 2021 ESPP will be increased on the first day of each fiscal year, beginning with fiscal year 2023, in an amount equal to the lesser of 1,020,000 shares of common stock, 1% of the outstanding shares of common stock on the last day of the immediately preceding fiscal year or such number of common shares determined by the board of directors. On January 1, 2024 and 2023, the number of shares of common stock that are available for sale under the 2021 ESPP was automatically increased by 592,523 and 570,258 shares, respectively.

Participating employees purchase stock under the 2021 ESPP at a price equal to the lower of 85% of the closing price on the applicable offering commencement date or 85% of the closing price on the applicable offering termination date. The 2021 ESPP provides for two offering periods of six months' duration with purchase periods terminating on either May 15 or November 15. Contributions under the 2021 ESPP are limited to a maximum of 15% of an employee's eligible compensation and a maximum of 3,000 shares during each purchase period. During the years ended December 31, 2023 and 2022, total stock-based compensation expense recognized related to the 2021 ESPP was $0.2 million. Additionally, during the years ended December 31, 2023 and 2022, a total of 27,440 and 21,157 shares of common stock were issued under the 2021 ESPP at an average per share price of $9.09 and $12.62, respectively.

9. Net Loss Per Share

Basic net loss per share of common stock is computed by dividing net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. The following table sets forth the computation of basic and diluted net loss per share attributable to common shareholders:

	Year ended December 31,	
	2023	2022
(in thousands, except share and per share amounts)		
Numerator:		
Net loss	$ (192,962)	$ (108,426)
Denominator:		
Weighted average shares of common stock outstanding, basic and diluted	58,542,974	52,471,003
Basic and diluted net loss per share attributable to common shareholders	$ (3.30)	$ (2.07)

The table below provides potentially dilutive securities not included in the calculation of the diluted net loss per share (in common stock equivalent shares) at December 31, 2023 and 2022, because to do so would be anti-dilutive.

	Year ended December 31,	
	2023	2022
Shares issuable upon exercise of stock options	10,338,724	7,592,856
Unvested restricted stock units	530,726	569,757
Unvested restricted stock awards	13,236	45,002
Shares purchasable under the 2021 Employee Stock Purchase Plan	64,823	11,294
Total	10,947,509	8,218,909

10. Employee Benefit Plan

Effective March 1, 2021, the Company assumed a defined contribution 401(k) plan from a related party—Kalika Biosciences, Inc. ("Kalika") for employees who are at least 21 years of age. Employees are eligible to participate in the plan beginning on the first day of employment. Under the terms of the plan, employees may make voluntary contributions as a percentage of compensation.

In December 2021, the Company amended the 401(k) plan, effective February 15, 2022, and added a provision for an employer matching contribution in the amount of 50% of the first 8% of employee contributions to the 401(k) plan. In February 2022, the Company further amended the 401(k) plan, effective March 31, 2022, to adjust the vesting schedule related to the employer matching contributions. The vesting schedule for employer matching contributions was changed to a 3-year graded vesting schedule, with contributions vesting 35%, 70% and 100% at the ends of the first, second and third years of employment with the Company, respectively. Company contributions under the 401(k) plan were $0.5 million and $0.2 million for the years ended December 31, 2023 and 2022, respectively.

11. Income Taxes

Income tax expense for both domestic and foreign operations was immaterial for the years ended December 31, 2023 and 2022. The Company included income tax expense in general and administrative expenses and other (income) expense in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, respectively.

The amount of net loss before provision for income taxes for the years ended December 31, 2023 and 2022 is as follows (in thousands):

	Year ended December 31,	
	2023	2022
U.S. net loss before income taxes	$ (121,383)	$ (52,073)
Foreign net loss before income taxes	(71,548)	(56,353)
Net loss before income taxes	$ (192,931)	$ (108,426)

A reconciliation of the federal statutory rate to the effective tax rate for loss from continuing operations for the years ended December 31, 2023 and 2022 is as follows:

	Year ended December 31,	
	2023	2022
% of pre-tax loss:		
Statutory federal income tax rate	21.0%	21.0%
Foreign rate differential	1.5%	2.1%
Foreign non-deductible interest expense	-0.6%	0.0%
Prior year adjustments	3.5%	0.7%
Officers compensation limitation	-2.0%	-2.0%
Stock compensation	1.7%	2.0%
Research and development credits	2.5%	2.1%
Other	0.0%	0.1%
Valuation allowance	-27.6%	-26.0%
Effective income tax rate	0.0%	0.0%

Significant components of the deferred tax balances at December 31, 2023 and 2022 are presented below (in thousands):

	December 31,	
	2023	2022
Deferred tax assets:		
Net operating losses	$ 52,827	$ 29,180
Stock compensation	4,845	1,995
Research and development credits	8,874	4,096
Research and development expenses	30,321	8,036
Unrealized (gain) loss on marketable securities	(6)	229
Operating lease liabilities	2,620	310
Other	1,073	1,467
Total gross deferred tax assets	100,554	45,313
Valuation allowance	(98,073)	(44,997)
Total deferred tax assets, net	2,481	316
Deferred tax liabilities:		
Property and equipment	(71)	(10)
Operating lease right-of-use assets	(2,410)	(306)
Total deferred tax liabilities	(2,481)	(316)
Net deferred tax assets	$ —	$ —

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company maintains a valuation allowance for its net deferred tax assets due to the uncertainty that such assets will be realized and evaluates the recoverability of its deferred tax assets on at least an annual basis. The Company has determined that its deferred tax assets are not realizable due to a lack of certainty regarding projected future profits.

For the years ended December 31, 2023 and 2022, the Company had federal net operating loss (“NOL”) carryforwards of $30.4 million and $27.9 million, respectively. The losses do not expire, but are limited to 80% utilization against taxable income. For the years ended December 31, 2023 and 2022, the Company had United Kingdom (“U.K.”) pre-trading expenditures of approximately $185.8 million and $93.3 million, respectively. Tax relief for pre-trading expenditures is generally limited to the expenditures incurred in the seven years prior to trade commencing.

Due to the Company's history of losses and uncertainty regarding future earnings, a valuation allowance has been recorded against the Company's deferred tax assets, as it is not more likely than not that such assets will be realized.

Pursuant to Internal Revenue Code (“IRC”) of 1986, as amended specifically IRC Section 382, the Company’s ability to use U.S. net operating loss carryforwards to offset future taxable income is limited if the Company experiences a cumulative change in ownership of more than 50% within a three-year testing period. The Company has not completed an ownership change analysis pursuant to IRC Section 382 as of December 31, 2023. If ownership changes within the meaning of IRC Section 382 are identified as having occurred, the amount of remaining net operating loss carryforwards available to offset future taxable income and income tax expense in future years may be significantly restricted.

As of December 31, 2023, the Company had federal research and development tax credits of $8.2 million, that will begin to expire in 2039. At December 31, 2023, the Company had state research and development credits of $3.1 million, that do not expire.

A reconciliation of the beginning and ending amount of unrecognized tax benefits for the year ended December 31, 2023 is as follows (in thousands):

	December 31,	
	2023	2022
Balance at beginning of period	$ 1,208	$ —
Increase (decrease) related to prior year tax positions	(717)	348
Increase related to current year tax positions	1,378	860
Balance at end of period	$ 1,869	$ 1,208

The Company accounts for its unrecognized tax benefits in accordance with ASC 740. The Company's policy is to recognize interest and penalties that would be assessed in relation to the settlement value of unrecognized tax benefits as a component of income tax expense. At December 31, 2023 and 2022, the Company did not recognize any interest and penalties. The amount of unrecognized tax benefit, if recognized and realized, that would affect the effective tax rate is $1.8 million as of December 31, 2023. The Company does not expect there would be unrecognized tax benefits that will significantly increase or decrease within 12 months of the reporting date.

The Company is not currently under tax examination in any tax jurisdiction. At December 31, 2023, the Company remains subject to income tax examinations in the U.S. and in the U.K. for tax years 2020 through 2023. The Company's tax years from inception are subject to examination in the U.S. and in the U.K. due to historical losses and tax attributes.

12. Related Party Transactions

On October 17, 2019, the Company entered into a Research and Development Support Services Agreement with Bayside Pharma, LLC ("Bayside") that outlined the terms of services provided by Bayside to the Company, as well as the fees charged for such services. Bayside is a research and development services company that provides certain research and development support services and facilities. Bayside is owned by an employee of the Company. The Company pays Bayside monthly for costs incurred under the agreement. Either party may terminate the support services agreement by giving 30 days' prior notice.

Expense recognized by the Company under the related party Support Services Agreements was as follows (in thousands):

	Year ended December 31,	
	2023	2022
Research and development - Bayside	$ 1,023	$ 883
Total research and development - related party	$ 1,023	$ 883

At December 31, 2023 and 2022, the Company had accounts payable and accrued expenses due to related parties of $0.1 million. At December 31, 2023 and 2022, the Company had an immaterial amount of prepaid expenses to related parties.

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EXECUTIVE TEAM

Raju Mohan, Ph.D.
President and Chief Executive Officer

Martin Auster, M.D.
Chief Financial Officer

John Nuss, Ph.D.
Chief Scientific Officer

BOARD OF DIRECTORS

Sheila Gujrathi, M.D.
Executive Chair

Onaiza Cadoret-Manier
Director

Allison J. Hulme, Ph.D.
Director

Somu Subramaniam
Director

William White, J.D.
Director

Raju Mohan, Ph.D.
Director

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ANNUAL MEETING OF STOCKHOLDERS
Wednesday, June 5, 2024 10:00 am, Pacific Time

COMMON STOCK LISTING
NASDAQ Global Select Market Ticker Symbol: VTYX

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INDEPENDENT AUDITORS
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LEGAL COUNSEL
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San Diego, California

NOTE ON FORWARD LOOKING STATEMENTS
This annual report contains forward-looking statements within the meaning of the United States securities laws. Such forward-looking statements are subject to risks and uncertainties that could cause Ventyx Biosciences, Inc. actual results to differ materially from those indicated by these forward-looking statements. Information on the risks and uncertainties that could affect Ventyx Biosciences, Inc. results is included in the Annual Report on Form 10-K included herewith and other filings with the SEC. Ventyx Biosciences, Inc. undertakes no obligation to update any forward-looking statements.

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