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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2024

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 001-39402

ANNEXON, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**27-5414423**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(Address of principal executive offices including zip code)
Registrant's telephone number, including area code: (650) 822-5500

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ANNX	The Nasdaq Stock Market

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

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 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 Exchange Act). Yes ☐ No ☒

As of June 28, 2024, the aggregate market value of the Registrant's Common Stock held by non-affiliates of the Registrant (based on the closing sales price of such shares on the Nasdaq Global Select Market on June 28, 2024) was approximately $477.2 million. For purposes of calculating the aggregate market value of shares held by non-affiliates, we have assumed that all outstanding shares are held by non-affiliates, except for shares held by each of our executive officers, directors and 10% or greater stockholders. This calculation does not reflect a determination that such parties are affiliates for any other purpose.

The number of shares of the Registrant's Common Stock outstanding as of February 28, 2025 was 109,709,826. This number does not include 38,543,577 shares of Common Stock issuable upon the exercise of pre-funded warrants (which are immediately exercisable at an exercise price of $0.001 per share of Common Stock, subject to beneficial ownership limitations). See Note 6—*Stockholders' Equity* to the Registrant's audited consolidated financial statements.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our expectations regarding the potential market size and size of the potential patient populations for our product candidates and any future product candidates, if approved for commercial use;
- our clinical and regulatory development plans;
- our expectations with regard to the initiation, scope, rate of progress, enrollment, dosing and results of our clinical studies, preclinical studies and research and development programs, including the timing and availability of data from such studies;
- the timing of commencement of future nonclinical studies, preclinical studies and clinical trials and research and development programs;
- our ability to acquire, discover, develop and advance product candidates into, and successfully complete, clinical trials;
- our intentions and our ability to establish collaborations and/or partnerships;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- our commercialization, marketing and manufacturing capabilities and expectations;
- our intentions with respect to the commercialization of our product candidates;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model and strategic plans for our business and product candidates, including additional indications for which we may pursue;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, including the projected terms of patent protection;
- estimates regarding the sufficiency of our cash resources and our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
- the potential future sales of our common stock under our at-the-market offering program;
- our future financial or operating performance;
- developments and projections relating to our competitors and our industry, including competing products; and
- our plans, objectives, expectations and initiations and any other statements that are not historical facts.

We have based these forward-looking statements largely on our current expectations, estimates, forecasts and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the sections titled "Summary Risk Factor," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this Annual Report on Form 10-K for a discussion of important factors that may cause our actual results

to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed as exhibits completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this Annual Report on Form 10-K by these cautionary statements.

SUMMARY RISK FACTORS

The following summarizes the most material risks that make an investment in our securities risky or speculative. If any of the following risks occur or persist, our business, financial condition and results of operations could be materially harmed and the price of our common stock could significantly decline.

- We are a clinical-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability.
- We will require substantial additional financing to achieve our goals, 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 programs, commercialization efforts or other operations.
- Our business is heavily dependent on the successful development, regulatory approval and commercialization of our product candidates, some of which are in early stages of clinical development.
- Research and development of biopharmaceutical products is inherently risky. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.
- We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect.
- We conduct, and in the future plan to conduct, clinical trials for product candidates outside the United States, and the U.S. Food and Drug Administration, or FDA, and comparable foreign regulatory authorities may not accept data from such trials.
- Adverse events or undesirable side effects caused by, or other unexpected properties of, any of our product candidates could halt their clinical development, delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.
- We rely on third-party suppliers to manufacture our product candidates, and we intend to rely on third parties to produce commercial supplies of any approved product. The loss of these suppliers, or their failure to comply with applicable regulatory requirements or to provide us with sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.
- The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.
- Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.
- If we are unable to obtain, maintain and enforce intellectual property protection directed to our current and any future technologies that we develop, others may be able to make, use or sell products substantially the same as ours, which could adversely affect our ability to compete in the market.
- Our stock price has been volatile, and could in the future be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.
- Actual or perceived failure to comply with applicable data protection laws, regulations, standards, contractual obligations and other requirements related to data privacy and security could lead to government enforcement actions and civil or criminal penalties, private litigation (including class actions) or adverse publicity and otherwise could negatively affect our results of operations and business.

[This page intentionally left blank]

PART I

Item 1. Business.

In this Annual Report on Form 10-K, "we," "our," "us," "Annexon" and the "Company" refer to Annexon, Inc. and its consolidated subsidiary. Annexon, Annexon, Inc., the Annexon logo and other trade names, trademarks or service marks of Annexon are the property of Annexon, Inc. This report contains references to our trademarks and to trademarks belonging to other entities. Trade names, trademarks and service marks of other companies appearing in this report are the property of their respective holders. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Overview

We are a clinical-stage biopharmaceutical company pioneering a new class of complement medicines for people living with devastating inflammatory-related diseases. The classical complement pathway is a core component to the body's immune system that activates a powerful inflammatory cascade. We believe that by stopping the classical complement pathway at its start by targeting C1q, the initiating molecule of the classical complement pathway, our approach may have the potential to provide more complete protection against complement-mediated disorders of the body, brain and eye.

Using our proprietary platform, we are identifying and characterizing the role of the classical complement pathway in three therapeutic areas—autoimmune, neurodegeneration and ophthalmology. In so doing, we are advancing a pipeline of product candidates designed to block the early classical cascade and all downstream pathway components and their tissue-damaging functions. Our goal is to suppress excessive or aberrant classical complement activity that contributes to chronic inflammation and tissue damage to slow or even halt disease progression, while preserving the beneficial immune functions of the lectin and alternative complement pathways involved in the clearance of pathogens and damaged cells. We have demonstrated robust target engagement in the body, brain and eye, and clinical proof of concept in multiple diseases, and have focused our resources on development of three priority programs:

- **Guillain-Barré Syndrome, or GBS:** We are advancing our lead candidate, ANX005, an investigational, full-length monoclonal antibody, or mAb, formulated for intravenous administration as the potential first targeted treatment for patients with GBS. GBS is a rare antibody-mediated autoimmune disease that is the most common cause of acute neuromuscular paralysis, with no therapies in the United States approved by the FDA. We believe maximum suppression of C1q and the classical complement cascade early in the disease process may act to rapidly prevent complement-mediated nerve damage and irreversible neurological disability. In a prior Phase 1b placebo-controlled proof-of-concept trial, a single dose of ANX005 showed rapid and consistent improvement in muscle strength that translated into observable gains in health status, including a reduction in the need of mechanical ventilation, as well as a reduction in nerve damage and clinical function. In 2024, we completed a Phase 3 trial in 241 patients, which showed ANX005 helped patients improve sooner with rapid increase in muscle strength and more complete functional recovery than placebo through six months, and provided an important benefit in the burden of care by enabling patients to walk or be off ventilation earlier. In addition, we completed a Real World Evidence, or RWE, study that matched ANX005-treated patients from the Phase 3 study with a western world patient population from the International Guillain-Barré Syndrome Outcomes Study, or IGOS, predominantly from Europe and North America treated with current standards of care (intravenous immunoglobulin, or IVIg, or plasma exchange, or PE). Consistent with the Phase 3 trial, ANX005 showed a rapid increase in muscle strength with more complete recovery over IVIg or PE. We anticipate the Phase 3 and RWE results to support a comprehensive dataset for our Biologics License Application, or BLA, and are targeting the first half of 2025 for our pre-BLA meeting with the FDA ahead of our planned BLA submission. ANX005 has been granted Fast Track and orphan drug designation for the treatment of GBS from the FDA. ANX005 has also been granted orphan designation from the European Medicines Agency, or EMA.
- **Geographic Atrophy, or GA:** We are advancing ANX007, an antigen-binding fragment, or Fab, formulated for intravitreal administration, as the first potential program with a global registration path to

approval in Europe and the United States for the treatment of dry AMD with GA. Dry AMD with GA is a leading cause of vision loss in the elderly, that affects more than an estimated eight million people globally, and there are no approved therapies targeting the preservation of vision in this disease. ANX007 is designed to block C1q locally in the eye, to provide more complete protection against excess classical complement activity and the loss of photoreceptor neurons. It is the only investigational therapy in GA to show significant vision preservation on assessments of best corrected visual acuity, or BCVA, and low luminance visual acuity, or LLVA, demonstrating significant protection from vision loss in both normal and low light conditions, as well as significant preservation of central retinal photoreceptors necessary for visual acuity as demonstrated in the Phase 2 ARCHER trial. In 2024, we initiated our Phase 3 ARCHER II trial, a global, sham-controlled, double-masked trial expected to enroll ~630 patients who have dry AMD with GA. The primary endpoint of ARCHER II is prevention of ≥15-letter loss of BCVA, and a secondary objective structural measure is prevention of ellipsoid zone (EZ) loss. The single-study program will be analyzed as two sub-studies for the U.S. in accordance with the FDA's two-trial recommendation. Accordingly, Annexon no longer plans to conduct a second injection-controlled head-to-head Phase 3 trial. We expect to complete enrollment of ARCHER II in the second half of 2025 and report topline data in the second half of 2026. ANX007 is the first and only therapeutic candidate for the treatment of GA to receive Priority Medicine, or PRIME, designation by the EMA, which provides early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options.

- **ANX1502 for Autoimmune Indications:** We are advancing ANX1502, a novel oral small molecule inhibitor of classical complement which we believe is first-in-kind. In a Phase 1 single-ascending dose, or SAD, and multiple-ascending dose, or MAD, clinical trial in healthy volunteers designed to evaluate the safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD, ANX1502 was generally well tolerated across cohorts with no serious adverse events, achieved target levels of active drug and showed supportive impact on a PD biomarker of complement activity that support its advancement. We are evaluating a tablet formulation of ANX1502 in an ongoing proof-of-concept study in patients with cold agglutinin disease, or CAD, to assess PK, PD and clinical efficacy endpoints (e.g., hemolysis as measured by reduction of elevated bilirubin) and data are expected in mid-2025. Following the successful completion of the proof-of-concept study, we intend to evaluate ANX1502 in serious complement-mediated diseases, with the aim of providing enhanced efficacy and offering convenient dosing administration for long-term treatment of chronic autoimmune conditions.

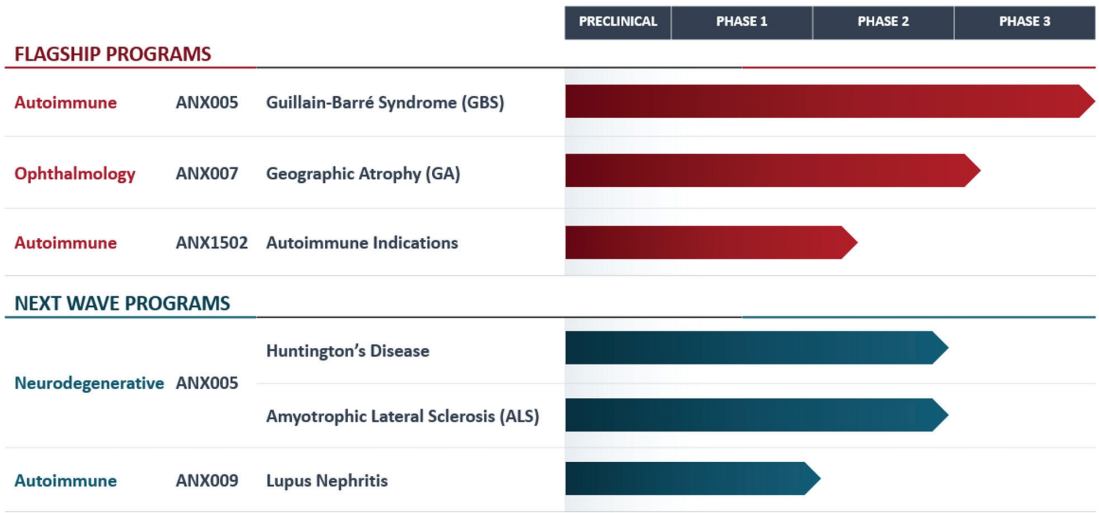
Annexon was co-founded by the late Dr. Ben Barres, former member of the National Academy of Sciences, Chair of Neurobiology at Stanford University and a pioneer in complement-mediated neurodegeneration, and Dr. Arnon Rosenthal, a world-renowned scientist and industry executive. We have assembled a seasoned and accomplished management team that has been involved in the discovery, development, approval and commercialization of numerous marketed drugs, and has been studying the complement pathway and autoimmune and neurodegenerative disorders for decades. Our team is further supported by an experienced scientific advisory board, board of directors and leading healthcare investors that share our commitment to advancing transformative medicines for patients suffering from debilitating autoimmune and neurodegenerative diseases.

We hold worldwide development and commercialization rights, including through exclusive licenses, to all of our product candidates, which allows us to strategically maximize value from our product portfolio over time. Our patent portfolio includes patent protection for our upstream complement platform and each of our product candidates.

Our Pipeline

Our pipeline is led by three flagship programs focused on complement-mediated diseases of the body, brain and eye for which there is significant unmet medical need and where we have the potential to provide a first-in-class treatment opportunity. Beyond our flagship programs, our "next wave" programs are supported by a strong scientific

and clinical rationale and poised for advancement following availability of resources and ongoing evaluation of further development options. Our clinical-stage pipeline is summarized below:



In addition to our flagship programs in GBS, dry AMD with GA and ANX1502 for autoimmune indications, we continue to be encouraged by multiple "next wave" programs, which provide additional potential portfolio growth and diversification.

We have evaluated ANX005 in patients with Huntington's Disease, or HD, and amyotrophic lateral sclerosis, or ALS, chronic neurodegenerative disorders in which aberrant classical complement activation drives neuroinflammation and has been shown to be associated with disease progression. In a completed Phase 2 clinical trial in patients with manifest HD, chronic dosing of ANX005 was generally well-tolerated, demonstrated rapid and sustained target engagement of C1q in both blood and cerebrospinal fluid, or CSF, reduced downstream complement markers in CSF, and showed promising efficacy signals on standard measures of disease progression in patients with higher levels of classical complement activity at baseline.

In a completed signal-finding open-label Phase 2a trial in patients with ALS, chronic dosing of ANX005 was generally well-tolerated, showed rapid and sustained target engagement of C1q in blood, and reduced downstream pharmacodynamic complement markers in blood. Consistent with what has been shown in other neurodegenerative diseases, including HD, exploratory analyses indicated that patients with higher baseline classical complement activation who enrolled within 12 months of diagnosis achieved better outcomes, including less functional decline on the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) and stabilization of neurofilament light chain (NfL). These analyses support a precision medicine approach to identify patients most likely to respond to anti-C1q therapy in clinical trials with recently diagnosed ALS patients who have elevated baseline levels of classical complement activity.

In addition, we have developed ANX009, a C1q-blocking Fab formulated for subcutaneous delivery, for patients with lupus nephritis, or LN, who have high baseline complement activity. LN is an autoimmune disease for which pathogenic anti-C1q antibodies, or PACAs, enhance activity and uniquely amplify kidney inflammation and damage. In a completed Phase 1b signal-finding trial, ANX009 was well tolerated, demonstrated plasma C1q target engagement and complement inhibition, and rapidly increased free/circulating PACA levels (consistent with decreased deposition in the kidney) and improved all downstream markers of complement consumption and activation (C4, as well as C3 and C5b-9).

We are evaluating options for future development of ANX005 in chronic neurodegenerative indications and ANX009 in LN.

Our Strategy

Our goal is to develop disease-modifying medicines for patients suffering from classical complement-mediated diseases of the body, brain and eye. Key elements of our strategy include:

- ***Leveraging our distinct approach of inhibiting C1q and aberrant classical complement activity to address a broad range of well-characterized classical complement-mediated diseases of the body, brain and eye.*** By inhibiting C1q and the early classical cascade, we believe our product candidates are uniquely designed to address a wide range of antibody-mediated autoimmune diseases and complement-mediated neurodegenerative disorders. We believe full classical complement inhibition may result in clinical benefits by blocking aberrant upstream and downstream immune cell activation in our targeted indications, as well as potentially provide safety advantages by leaving the lectin and alternative pathways intact to perform their normal immune functions.

- ***Prioritizing resources and execution of mid- to late-stage development of three flagship programs.*** By focusing our resources on our three flagship programs in GBS, GA and ANX1502, our novel oral small molecule complement inhibitor, our goal is to create near-term value for patients, physicians and stakeholders.

- ***ANX005 for dry AMD with GBS: Prepare for BLA Submission and Commercialization, if approved.*** We are advancing ANX005 as the potential first targeted therapy for GBS, an acute neurological emergency for which there is no FDA approved treatment. ANX005 is being developed as a first-line monotherapy treatment option to address the global unmet needs of 150,000 patients annually diagnosed with GBS, in support of our goal of obtaining the first FDA-approval for the treatment of GBS. ANX005's well-tolerated, differentiated profile showing rapid and durable improvement in muscle strength, has received both Fast Track and orphan drug designations from the FDA, as well as orphan drug designation by the EMA.

- ***ANX007 for GA: Execute Global Registration Program.*** We are advancing ANX007 as the potential first program with a global registration path to approval for the treatment of dry AMD with GA in Europe and the United States to address the unmet needs of more than 8 million patients worldwide. ANX007's well-tolerated, differentiated profile is the only program to show significant protection against vision loss as well as significant protection of central retinal photoreceptors necessary for visual acuity. ANX007 is the first and only therapeutic candidate for the treatment of GA to receive PRIME designation in the EU, which provides early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options.

- ***ANX1502 for Autoimmune Disease: Advance First-in-Kind Oral Small Molecule Program.*** We are advancing an enhanced tablet formulation of ANX1502 designed to disrupt the complement-mediated autoimmune space as the potentially first orally available treatment. Following successful completion of the proof-of-concept study in patients with CAD, we intend to evaluate ANX1502 in serious complement-mediated diseases, with the aim of providing efficacy with enhanced dosing flexibility and convenience for long-term treatment of chronic autoimmune conditions.

- ***Expanding our portfolio across three therapeutics franchises informed by data from our flagship programs.*** We intend to leverage learnings and proof-of-concept data from our flagship programs to inform selection of additional patient populations involving classical complement-mediated diseases of the body, brain and eye. As we enhance our resources, we plan to efficiently prosecute opportunities across our three therapeutic franchises utilizing our disciplined, data-driven development strategy.

- ***Maximizing the value of our product candidates.*** We currently hold worldwide development and commercialization rights, including through exclusive licenses, to all of our product candidates. We have secured broad intellectual property protection for our upstream complement platform and intend to leverage our intellectual property and know-how to protect and enhance our leading position in developing novel therapeutics that target the classical complement cascade. We intend to pursue independent development and commercialization in indications and markets we can address with a focused sales and marketing organization. We plan to explore licensing agreements, collaborations or partnerships to advance our product candidates in indications and markets where we could accelerate and expand development and commercialization leveraging the resources of larger biopharmaceutical companies.

Overview of the Complement System and C1q Biology

The Complement System—three main complement pathways

The complement system is an integral component of the immune system that consists of many circulating and locally-produced molecules. This system evolved to enhance, or complement, other components of the adaptive and innate immune systems. The complement system, also known as the complement cascade, rapidly responds to pathogens, damaged cells and unwanted tissue components to facilitate their removal by the immune system.

There are three main complement pathways (also called cascades)—the classical, lectin and alternative pathways. Each pathway is initiated by different molecules that respond to distinct triggers. When activated, the initiating molecules set in motion a cascade of enzymatic reactions that greatly amplify, or complement, an inflammatory response. The classical pathway is initiated by C1q, which recognizes antibody complexes, specific pathogens, damaged cells or unwanted cellular components. The lectin pathway is triggered by carbohydrates on the surface of pathogens or cells. The alternative pathway amplifies the action of the other two pathways and also self-activates to eliminate pathogens or cells that are not specifically shielded by the body's built-in self-protective systems. While these three pathways are initiated by distinct molecules, they converge downstream on common pathway components known as C3 and C5.

Aberrant activation of the complement system can result in a range of diseases characterized by an attack on healthy tissue, such as red blood cells, nerve cells or kidney components. A broad range of diseases are known to be associated with pathological activation of the complement cascade, including antibody-mediated autoimmune disorders such as GBS, CAD and lupus nephritis, and complement-mediated neurodegeneration disorders in the eye, such as glaucoma and GA, and complement-mediated neurodegeneration disorders in the brain, such as HD, ALS, frontotemporal dementia and Alzheimer's disease. We believe intervening in the activation of the complement cascade offers a potent and selective mechanism for specifically slowing or reversing these disease processes.

Specific activated components of the complement cascade have important immune functions that contribute to three key outcomes:

- ***Immune cell recruitment and inflammation.*** Specific activated molecules from the cascade serve as soluble signals to make blood vessels leaky and attract immune cells into tissues.
- ***Directed immune cell attack.*** Several complement components, including C1q, bind directly to the pathogen and serve as receptors that direct immune cell attack and pathogen engulfment.
- ***Membrane damage.*** Downstream components of the cascade directly puncture the pathogen or cell surface, causing membrane damage and lysis.

Broad potential for classical complement pathway targeted therapeutics in autoimmune and neurodegenerative diseases

The classical complement cascade has a well-established role in augmenting antibody function within the immune system. C1q recognizes antibodies bound to pathogens or cells and activates the classical pathway to trigger their removal and clearance by the immune system. C1q can also directly recognize pathogens, damaged cells or unwanted cellular components leading to similar downstream clearance. A more recent finding made by the laboratory of Dr. Ben Barres, our scientific founder, is that C1q also directly interacts with neuronal connections, or synapses, during early development. Recognition of weaker synapses by C1q triggers the classical complement cascade and directs immune cells to "prune" the synapses away from neurons, thereby reinforcing stronger synapses to establish appropriate neuronal connections.

Because of its central role in immune function, aberrant activation of C1q can lead to damage of healthy tissue and destruction of functioning synapses. We are focused on two distinct disease processes involving C1q as a key mediator of tissue damage: antibody-mediated autoimmune disease and complement-mediated neurodegeneration.

In antibody-mediated autoimmune disease, self-reactive antibodies bind to cells or tissues, activating C1q and leading to damaging inflammatory responses. In GBS, pathogenic antibodies react with components of the peripheral nerve system, or PNS, to cause widespread peripheral nerve damage and paralysis. This disease process is also evident

in antibody-mediated autoimmune disease involving blood components, such as CAD, characterized by auto-reactive antibodies that trigger destruction of red blood cells, and in a subset of patients with systemic lupus erythematosus, or SLE, where endogenous pathogenic antibodies against C1q itself drive aberrant C1q activation and are highly associated with kidney damage, or lupus nephritis.

In complement-mediated neurodegeneration, aberrant activation of C1q at synapses in aging and disease can lead to excessive synapse loss and neuronal damage, driving disease progression in multiple neurodegenerative disorders regardless of the initiating factor. In animal models, C1q accumulated on synapses with age, building up to 300-fold higher levels than in younger animals. It did not activate with normal aging, but other inflammatory stimuli, including misfolded proteins, metabolic dysfunction or increases in intraocular pressure, appeared to aberrantly reactivate C1q's developmental role in synapse elimination. Complement activation and aberrant synapse pruning in disease may lead to neuroinflammation, loss of synaptic neuronal connections and neurodegeneration. In support of this hypothesis, we and other investigators have observed that C1q inhibition was protective in numerous models of neurodegenerative disease, including diseases of the eye, such as glaucoma and age-related macular degeneration, chronic diseases of the CNS, such as frontotemporal dementia, Alzheimer's, HD and Spinal Muscular Atrophy, or SMA, and acute injury, such as traumatic brain injury and stroke.

Our differentiated approach to treating complement-mediated autoimmune and neurodegenerative disease through inhibition of C1q

We believe that in order to selectively inhibit aberrant activation of the classical complement pathway implicated in driving certain complement-mediated autoimmune and neurodegenerative diseases, it is important to target the early components of the classical cascade, particularly C1q, C4 and C3. Activated fragments of C4 and C3 induce vascular leakiness and immune cell recruitment into the tissue, while other fragments of C4 and C3, as well as C1q, work together to direct immune cell attack to the cell or synapse surface. Furthermore, C1q inhibition blocks downstream classical pathway activation of C5 and its membrane damaging effects. We believe that inhibition of C1q does not block the activity of these components in the lectin or alternative complement pathways, and both of these pathways will continue to perform their normal immune functions.

Our Platform

Our novel upstream complement platform is designed to completely inhibit classical complement activity for the treatment of antibody-mediated autoimmune diseases and complement-mediated neurodegenerative diseases in the body, brain and eye. We believe there are potential advantages to our approach of upstream inhibition of the classical complement cascade, which include:

- ***Full inhibition of the classical cascade while preserving healthy immune function of the other complement pathways.*** Inhibition of C1q fully inhibits the classical cascade, including components downstream of C1q such as C4, C3, C5 and the downstream membrane attack complex. As a result, we believe our approach is designed to block all classical complement activity that can contribute to disease pathology, including immune cell recruitment, directed immune cell attack and membrane damage. By targeting upstream tissue-damaging components of the classical complement pathway, our approach leaves the lectin and alternative pathways to perform their normal immune function, which may aid both clinical improvement and safety. Our approach is also distinct from inhibiting C3 or C5. Inhibition of C5 will not affect the upstream components of the classical pathway involved in pathology (C1q, C4 and C3), while inhibition of C3 will block downstream components in all three complement pathways.
- ***Broad applicability across many indications.*** We believe our approach has broad utility for the treatment of diseases in which full inhibition of the entire classical complement cascade may be beneficial. We believe our approach is distinguishable from those that target only downstream complement components. Our initial indications represent our beachhead within antibody-mediated autoimmune and complement-

mediated neurodegenerative diseases, and we will selectively pursue both orphan and larger patient population diseases with clear biological evidence of classical complement activation.

Our Flagship Programs

Guillain-Barré Syndrome

Overview of Guillain-Barré Syndrome

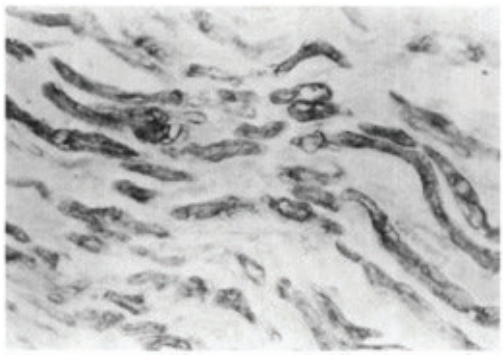
Guillain-Barré syndrome (GBS) is a serious and life-threatening condition that continues to be associated with significant long-term morbidity and mortality in patients despite use of IVIg treatment as standard of care. GBS is a rare disease, but is also the most common, most severe, and well understood acute paralytic inflammatory disease of the peripheral nervous system. GBS generally occurs post-infection in otherwise healthy persons. Antibodies generated against an infectious agent cross-react with components of peripheral nerves, leading to a complement mediated attack on nerve components, including myelin sheath and axonal tissue. The ensuing peripheral nerve damage is acute and rapidly progressive, leading to acute severe paralysis, significant morbidity, disability and mortality. The neuronal destruction progresses until titers of the cross-reactive, complement-activating antibodies have diminished (van den Berg et al., 2014). GBS impacts approximately 150,000 people annually worldwide, 22,000 in the United States and EU, and 7,000 are hospitalized each year in the United States. The prevalence of GBS continues to increase with advancing age. In 2004, the annual economic cost of GBS in the United States was $2 billion, largely due to the permanent disability and mortality it can cause.

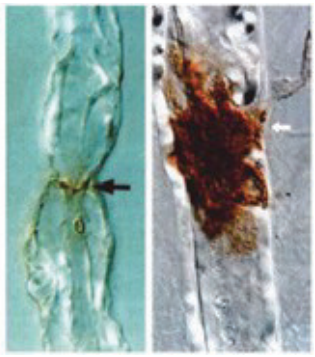
There are currently no FDA-approved or targeted therapies for the treatment of GBS. Treatment guidelines published by the American Academy of Neurology recommend early initiation of IVIg or plasma exchange in patients diagnosed with GBS. Although IVIg and plasma exchange are the established standards of care in the western world and parts of Asia, significant unmet need still exists, and many patients, despite receiving the standard of care, are left with residual neurological disability, accompanied by chronic pain and fatigue.

The clinical course of GBS usually involves rapidly progressive weakness in the limbs culminating in neuromuscular paralysis within two to four weeks of onset. According to 2011 estimates, 20 to 30% of patients require mechanical ventilation, over 20% have permanent motor or sensory disability and 2 to 20% of cases result in death globally. Many patients with GBS require extensive monitoring and supportive care and will seek treatment in a hospital within a few days of onset of the disease. Because approximately a quarter of patients need artificial ventilation due to respiratory muscle weakness, and many develop autonomic disturbances, admission in an intensive care unit is frequently necessary. Symptoms peak within four weeks as the auto-antibody response declines, followed by a recovery period that can last months or years, as the nervous system repairs itself. The development of targeted treatments for GBS is crucial to improve outcomes and quality of life for those affected by this debilitating condition.

C1q is a key driver of pathogenesis in GBS

GBS is an acute, autoimmune disease driven by antibodies that lead to activation of the classical complement cascade. Pathological nerve-targeting auto-antibodies, which may be triggered by an infection, lead to the activation of C1q and the classical complement cascade. Studies have shown that pathogenic auto-antibodies are present in the serum and CSF, and that activated components of the complement cascade are deposited on peripheral nerve tissue from GBS patients. Peripheral nerve roots are immersed in CSF as they emerge from the spinal cord and are prominent sites of damage in GBS. The figure below illustrates the activation of the classical complement pathway within peripheral nerves in GBS patient samples from autopsy. The left image shows a low magnification view of a peripheral nerve with numerous individual nerve fibers coated with membrane-damaging complement activation products (C5b-9; dark staining). The middle image shows a high magnification view of an individual nerve fiber with deposition of C3d (dark staining), a complement activation product that directs immune cell attack. The right image shows a highpower image of an individual nerve fiber being probed by an infiltrating immune cell (macrophage).





We believe that by blocking the activity of C1q early in the onset of the disease, we can minimize the neuronal damage caused by these pathogenic auto-antibodies, in turn reducing the patients' symptoms and accelerating their neurological recovery.

ANX005 Development Background in GBS

Since 2015, we have developed ANX005 as the potential first targeted therapy for patients with GBS, an acute neurological emergency for which there is no FDA approved treatment. ANX005 is being developed as a first-line monotherapy treatment option to address the unmet needs of GBS patients and healthcare providers, leveraging our expertise and leadership in classical complement-mediated diseases. A robust data package has been generated over the nine year development path that includes a placebo-controlled Phase 1b trial that established POC for ANX005 as a first-line treatment for GBS, a successful Phase 3 trial showing that ANX005 was generally well-tolerated and resulted in faster and more complete functional recovery versus placebo, a RWE study that showed improved outcomes against current standards of care in matched patient populations, and a drug-drug interaction study with ANX005 and IVIg strengthening the safety profile for ANX005 in GBS. Importantly, to ethically provide a placebo-controlled dataset, Annexon conducted ANX005's clinical development for GBS outside of the U.S. in jurisdictions where IVIg treatment is not readily available. In addition, Annexon has generated real-world evidence to support the generalizability of ANX005 to a matched Western patient population and compared ANX005 treatment outcomes from a single infusion of ANX005 versus standard of care IVIg given as a 5-day infusion or PE.

We have closely coordinated our clinical efforts with leading researchers of the International GBS Outcome Study, or IGOS, in pursuing a novel therapy for GBS. With the goal of aiding the development of effective treatments for GBS, practitioners established IGOS in May 2012, and have collected natural history data from 2,000 GBS patients worldwide. IGOS is a prospective, observational, multicenter cohort study that aims to identify the clinical and biological determinants and predictors of disease onset as well as the subtype, course and outcome of GBS. IGOS was established to help develop a better understanding of the mechanism of disease progression and recovery and to conduct selective therapeutic trials to improve patient outcomes. This natural history database is an invaluable resource to clinical development, facilitating the design of clinical trials, optimal selection of endpoints, and patient follow-up for one to three years. We initiated our GBS clinical development in Bangladesh, a country where the incidence of GBS is several times higher than in North America and Europe and where 17% of patients die from the disease and 20% suffer permanent disability and are unable to walk. Additionally, our site in Bangladesh is well situated to conduct clinical research in GBS in a manner compliant with good clinical practice, or GCP, requirements.

Phase 1b Trial of ANX005 in GBS

We conducted a Phase 1b placebo-controlled, dose escalation trial (n=50) of ANX005 in GBS patients at a tertiary care hospital in Bangladesh, in compliance with GCP as described above. The trial objectives included safety and tolerability, dosing levels and target engagement, and included a follow up of eight weeks. The dosing levels of ANX005 delivered in this trial ranged from 3 mg/kg to 75 mg/kg. ANX005 was well tolerated, and no drug-related serious adverse events or drug-related discontinuations occurred. The most common adverse events were acute infusion-related reactions, or IRRs, which occurred in the majority of patients and presented as low grade, non-serious, transient skin rash. These acute IRRs were mitigated by standard anti-inflammatory pre-medications.

Results from the Phase 1b trial showed increasing serum levels of ANX005 and its duration in the circulation at increasing dose levels, and that the drug was present in the serum for up to three weeks at a dose of 75 mg/kg. When ANX005 was present in the circulation C1q function was fully inhibited, and rapidly returned to normal levels as ANX005 serum levels declined.

Much of the proximal weakness in GBS patients is due to involvement of peripheral nerve roots that are immersed in CSF as they exit the spinal cord. Hence, we believe product candidate levels and target inhibition in CSF may be an important contributor to efficacy. We observed that ANX005 entered the CSF of GBS patients treated with doses of 18-75 mg/kg of ANX005, resulting in full engagement of C1q inhibition in the CSF.

In the Phase 1b trial in GBS patients, ANX005 treatment at doses that engaged C1q in both serum and CSF (i.e., 18-75 mg/kg dose) resulted in a statistically significant early decline in serum NfL levels compared to placebo (two to four-week post treatment p-value <0.05). In this Phase 1b trial, we also explored the administration of ANX005 on multiple validated clinical disability measures including GBS-Disability Score, or GBS-DS, Medical Research Council Muscle Strength Scale, or MRC, and Inflammatory Rasch-built Overall Disability Scale, or I-RODS, over an eight-week period. We observed that early decline in NfL correlated with improvement in the GBS-DS at the end of the study (two to eight-week post treatment p-value <0.05). We believe these results suggest that ANX005 had a rapid impact on the disease process by ameliorating antibody-induced nerve damage, likely within the first two weeks of dosing.

Though the trial was not powered for statistical significance, treatment with ANX005 resulted in consistent, positive numerical trends, including an improvement in MRC score and the number of days of ventilation. We observed a dose-dependent trend for improvement in MRC within the first week of treatment.

Early improvement in MRC is known to have strong prognostic implications on long-term functional recovery (modified Erasmus GBS Outcome Score). In line with this published data, we found that early improvement in MRC correlated with patients' disability scores at the end of the Phase 1b trial (GBS-DS at week eight). This result is important because GBS-DS is typically used as the primary endpoint in GBS registrational studies. In addition, using a responder analysis, 28% of patients treated with high dose ANX005 (18-75 mg/kg) improved by at least three points on GBS-DS by week eight compared to 0% of placebo-treated patients.

Following the completion of the Phase 1b treatment cohorts (through 75 mg/kg), two unblinded exploratory cohorts were enrolled to establish higher dose and multiple dose safety and PK/PD to inform subsequent chronic dosing trials. These two exploratory cohorts were a single dose of 100 mg/kg, and two doses of 75 mg/kg separated by one week (150 mg/kg total). At these higher dose levels, ANX005 was well-tolerated, and no drug-related serious adverse events or drug-related discontinuations occurred; moreover, we did not reach a maximum tolerated dose. Similarly, we observed full inhibition of C1q in serum and CSF, a reduction in NfL and trends of improvement in clinical measures when compared to placebo; however, there was no additional impact on these clinical measures beyond that seen at 75 mg/kg.

The results of the Phase 1b dose-ranging trial in GBS showed that ANX005 was well-tolerated, fully inhibited C1q in the blood and CSF at target doses, and demonstrated an early reduction in NfL levels. Drug treatment was associated with a trend for early improvement in MRC, and early changes in MRC significantly correlated with improved clinical measures in GBS patients. An additional key learning from the study is the importance of using baseline MRC for patient stratification at the time of hospitalization and study entry. Accounting for baseline MRC strengthened the impact of ANX005 treatment in the biomarker and clinical measures, demonstrating that MRC will be an important stratification tool in future GBS trials.

Phase 3 Trial of ANX005 in GBS

Based on the positive findings from our Phase 1b trial, we conducted a randomized, double-blind, placebo-controlled, multi-center Phase 3 trial to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of ANX005 administered by a single intravenous, or IV, infusion. The Phase 3 trial enrolled 241 patients in Bangladesh and the Philippines diagnosed with GBS according to the National Institute of Neurological Disorders and Stroke Diagnostic Criteria for Guillain-Barré Syndrome at the onset of GBS-related weakness $\leq$10 days prior to the start of

treatment. Patients were stratified for leading prognostic factors including muscle strength and time from symptom onset.

In June 2024, we presented topline results from the Phase 3 trial demonstrating that a single infusion of ANX005 at 30 mg/met the trial's primary endpoint of a meaningful improvement in GBS-disability scale at week 8. Specifically, ANX005 30 mg/kg achieved a highly statistically significant 2.4-fold improvement on the GBS-DS (p = 0.0058), utilizing a proportional odds methodology to assess the proportion of patients who shift to better outcomes on the GBS-DS with ANX005 treatment compared to placebo at week 8. ANX005 30 mg/kg treatment also demonstrated improvements versus placebo on key secondary endpoints, including early gains in muscle strength by Medical Research Council (MRC) sum score at day 8 (p <0.0001*) and at week 8 (p = 0.0351*), and a median of 28 fewer days on artificial ventilation through week 26 (p = 0.0356*). Additionally, ANX005 30 mg/kg demonstrated a 31-day reduction in the median time to walk independently versus placebo (p = 0.0211*) in a prespecified analysis. ANX005 30 mg/kg treated patients got better sooner on each of these assessments, presenting important clinical care outcomes for patients and the healthcare community.

* nominal p-values

The Phase 3 trial evaluated two doses of ANX005, 30 mg/kg and 75 mg/kg, both of which delivered rapid and complete suppression of complement activity but differed in duration of C1q inhibition. The 30 mg/kg dose suppression lasted one week and the 75 mg/kg dose suppression lasted two to three weeks. ANX005 75 mg/kg outperformed placebo on multiple endpoints; however, it was not statistically significant on the primary endpoint of GBS-DS at week 8 (p = 0.5548). The two dose levels were evaluated based on findings in the earlier Phase 1b proof-of-concept study, which showed efficacy in pooled analysis of both shorter and longer duration of ANX005 C1q inhibition. Because classical complement drives tissue damage in the early phase of disease, while facilitating nerve repair after acute nerve injury, the strong positive Phase 3 results with the 30 mg/kg dose resulting in one week of C1q inhibition appeared to define the optimal treatment window.

The clinical safety and tolerability findings of ANX005 at both doses in the Phase 3 study support a generally well-tolerated profile with no new safety signals. The majority of adverse events were mild Grade 1 to moderate Grade 2 events. The most common treatment-related adverse events were infusion related reactions (30.4%) that were mostly mild transient rashes. There were no autoimmune related adverse events, and no drug-related deaths or serious infections were observed.

Real World Evidence Study of ANX005 in GBS

All of our studies to date for ANX005 in GBS have been conducted at sites outside the United States. To support these clinical trials and based on feedback from the FDA, we conducted a RWE study in collaboration with IGOS investigators to establish comparability between Phase 3 participants and western patients.

IGOS investigators and we established a cohort of 79 real-world patients from the IGOS global patient registry that was matched based on key prespecified prognostic factors to the cohort of 79 patients treated with ANX005 30 mg/kg from our completed Phase 3 study. Patients in the ANX005 Phase 3 population had moderate to severe disease, and the matching level demonstrates that the Phase 3 population is represented within the global GBS patient spectrum captured in IGOS.

This RWE study also provided the first insights comparing ANX005 with the standard of care IVIg or PE. Patients treated with ANX005 showed faster and greater improvement in muscle strength and disability compared to patients in the matched IGOS cohort treated with IVIg or PE. The comparison also showed that fewer patients treated with ANX005 required mechanical ventilation. Further, ANX005-treated patients were observed to spend less time on ventilation and less time in the intensive care unit, or ICU. These findings indicate that ANX005 may decrease the overall burden of GBS care.

Some key findings comparing ANX005 30 mg/kg to IVIg or PE included:

- By week 1, patients treated with ANX005 showed more than 10-point improvement in muscle strength over patients treated with IVIg or PE, a clinically meaningful benefit as measured by MRC sumscore and an indicator for future recovery potential (p < 0.0001).

- Patients treated with ANX005 were approximately twice as likely to be in a better state of health than patients on IVIg or PE on the GBS-DS at multiple timepoints throughout the study, including at week 8, the primary endpoint for the Phase 3 trial ($p = 0.0459$).
- Approximately half the number of patients treated with ANX005 (n=15 of 79) required mechanical ventilation compared with patients treated with IVIg or PE (n=32 of 79) ($p = 0.022$).
- ANX005-treated patients were observed to spend fewer days on mechanical ventilation and fewer days in the ICU (median of 12 fewer days for each measure, p = n.s.).

Together, we believe the Phase 3 trial and RWE study demonstrate consistent, robust effects of ANX005 treatment in support of a potential U.S. BLA. ANX005 has received both Fast Track and orphan drug designations from the FDA as well as orphan designation by the EMA for the treatment of GBS. The EMA orphan designation was based on an indirect comparison between ANX005 and IVIg that demonstrated a notable and early improvement in muscle strength with ANX005 versus patients treated with IVIg, which translated into observable gains in health status, including a reduction in the need of mechanical ventilation.

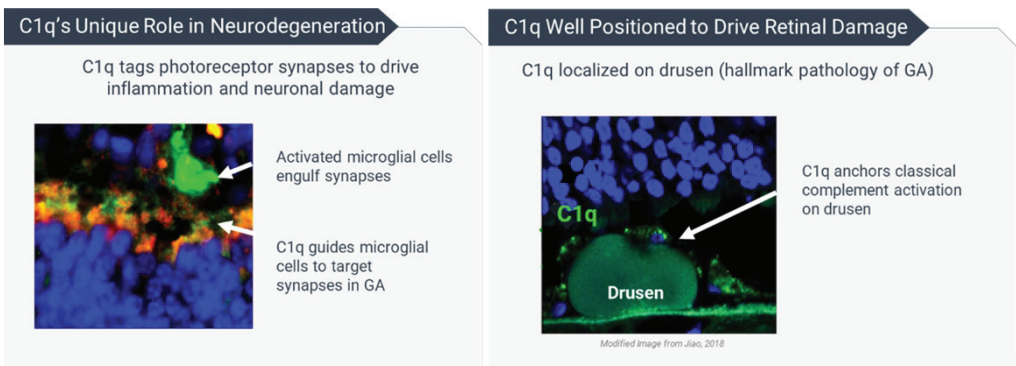
Geographic Atrophy

Overview of Geographic Atrophy

GA is an advanced form of dry age-related macular degeneration (AMD), an eye disease that is the leading cause of blindness in the elderly. GA is a chronic progressive neurodegenerative disorder of the retina involving the loss of photoreceptor synapses and cells in the outer retina. GA affects an estimated one million people in the United States and eight million people globally, severely limiting their independence and causing frustration, anxiety and emotional hardship. Effective treatments that preserve vision are still needed, as no currently approved therapies have been shown in clinical trials to significantly prevent vision loss.

Role of C1q and Complement in Geographic Atrophy

Genome-wide association studies have strongly implicated multiple components of the complement cascade in AMD and geographic atrophy. For example, specific alleles of the gene for C3 can increase the likelihood of developing AMD by 50%. Histopathological investigations have also observed the presence of complement components in geographic atrophy. These studies largely point to a role of excessive C3 activity in disease, but do not indicate how C3 is being activated (classical, lectin or alternative pathways). We have identified a potential dual role of C1q and the classical cascade as an important complement-activating system in geographic atrophy. First, we found that C1q strongly accumulated on photoreceptor cell synapses with normal age or disease, as shown below (left panel), implicating C1q's role in excessive synapse pruning and complement-mediated neurodegeneration. Second, C1q and C1q ligands, such as C-reactive protein, also accumulated in the retina below photoreceptor cells in association with drusen (extracellular membrane and protein debris associated with geographic atrophy; right panel). These results suggest that the photoreceptor neurons and pigmented retinal epithelial cells – cell types that are both lost in GA – are sandwiched between deposits of C1q and that the classical complement cascade may have an ongoing and pathogenic role in GA by activating C3.



In support of this hypothesis, we found that either deletion or pharmacologic inhibition of C1q was protective in an animal model of photoreceptor neuron loss induced by photo-oxidation, as shown below. Further, components of the classical complement cascade have been associated with photoreceptor cells in human GA tissue (C4 and C3) and implicated in photoreceptor cell targeting with an in vitro assay. Finally, C1q is locally produced within the retina during disease by infiltrating immune cells, indicating that its pathogenic role may be amenable to local inhibition of C1q. As described above, we believe inhibition of C1q would block all key components of the classical cascade, including C1q, C4, and C3 involved in immune cell attack and synapse pruning, as well as C5 involved in direct membrane damage.

C1q inhibition was shown to be protective of photoreceptor cells and retinal function in a model of photoreceptor cell damage induced by light.

Phase 1b Trial of ANX007 in Glaucoma to Support Development in GA

We completed single-ascending dose (n=9) and sham-controlled multiple dose (n=17) studies of intravitreal ANX007 in patients with glaucoma to evaluate safety, tolerability, pharmacokinetics and target engagement. These patients had aqueous humor taps so that ocular fluid could be analyzed for levels of ANX007 and free C1q immediately prior to first dose (day 1) and prior to second dose (day 29). The studies showed that ANX007 was well-tolerated at all doses (1 mg, 2.5 mg and 5 mg) and achieved complete suppression of C1q at 2.5 mg and 5 mg.

Phase 2 ARCHER Trial of ANX007 in GA

We conducted the randomized, multi-center, double-masked, sham-controlled Phase 2 ARCHER trial to compare the safety and efficacy of ANX007 in patients with GA secondary to AMD. The study enrolled a total of 270 patients, stratified by GA lesion size, location and choroidal neovascularization, or CNV, in the fellow eye at the time of enrollment. Patients were nearly equally split between foveal (49.4% to 57.3%) and non-foveal groups, had an average age of 80 years and were balanced between female and male. Ninety-six percent of patients enrolled were from the United States. Patients were randomized to receive an intravitreal dose of 5mg ANX007 monthly (n=89), 5mg ANX007 every other month (n=92) or sham monthly or every other month (pooled n=89) for a treatment period of 12 months, followed by a six-month off-treatment period.

The primary outcome measure of the study was the rate of change in GA lesion growth (slope) from baseline as measured by fundus autofluorescence through 12 months for the study eye. The study included multiple pre-specified visual function measures to assess the effects of ANX007 on vision: change from baseline in BCVA; change from baseline in low-luminance best corrected visual acuity; and change in baseline from low-luminance visual acuity deficit, or LLVD.

In the Phase 2 ARCHER trial, ANX007 demonstrated consistent protection against vision loss in a broad population of patients with GA. Specifically, topline data from the Phase 2 ARCHER trial reported in May 2023 and presented at the American Society of Retina Specialists Annual Meeting in July 2023 showed that ANX007 provided significant, time and dose-dependent protection from vision loss in patients with GA, measured by BCVA ≥ 15-letter loss, the widely accepted and clinically meaningful functional endpoint assessing visual acuity.

Monthly treatment with ANX007 demonstrated nominally statistically significant reduction in BCVA ≥15-letter loss (p=0.0021) compared to sham. The persistent ≥15-letter BCVA loss through month 12 hazard was reduced 72% in the monthly arm (p=0.006) and 48% in the every other month arm (p=0.064). Protection from vision loss was also shown in multiple additional prespecified measures of BCVA and visual function, including in standard and low light conditions. Protection from vision loss was enhanced in a subpopulation of patients with less advanced disease defined by LLVD < 30 at baseline and in patients with more intact vision as defined by <80% ellipsoid zone, or EZ, loss. ANX007's treatment effect increased over the course of the on-treatment portion of the study, suggesting that ANX007 may provide a growing and durable treatment effect over time. While benefit gained against vision lost was maintained during the subsequent six-month off-treatment period, the rate of decline for BCVA ≥ 15-letter vision began to parallel that of sham, providing additional support for the observed on-treatment protection.

While the primary endpoint of mean rate of change (slope) in GA lesion area compared to sham at 12 months did not reach statistical significance, greater impact on retinal pigment epithelium loss was observed in the second six months of treatment versus the first. Consistent with its proposed mechanism, ANX007 reduced photoreceptor EZ loss and showed more pronounced effect in reducing total EZ loss and protection of photoreceptors in the central fovea that are associated with visual acuity.

ANX007 treatment was generally well-tolerated, with no increase in CNV rates between the treated and sham arms and no events of retinal vasculitis reported.

Phase 3 Program of ANX007 in dry AMD with GA

In 2024, we initiated the Phase 3 ARCHER II trial, a global, sham-controlled, double-masked trial enrolling approximately 630 patients who have dry AMD with GA. The single-study program will be analyzed as two sub-studies in the U.S. in accordance with the FDA's two-trial recommendation. The primary endpoint of ARCHER II is prevention of ≥15-letter loss of BCVA, and an objective secondary objective structural measure is prevention of EZ loss. Accordingly, Annexon no longer plans to conduct a second injection-controlled head-to-head Phase 3 trial.

ANX007 is the first therapeutic candidate for the treatment of GA to receive PRIME designation by the EMA, which provides early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options.

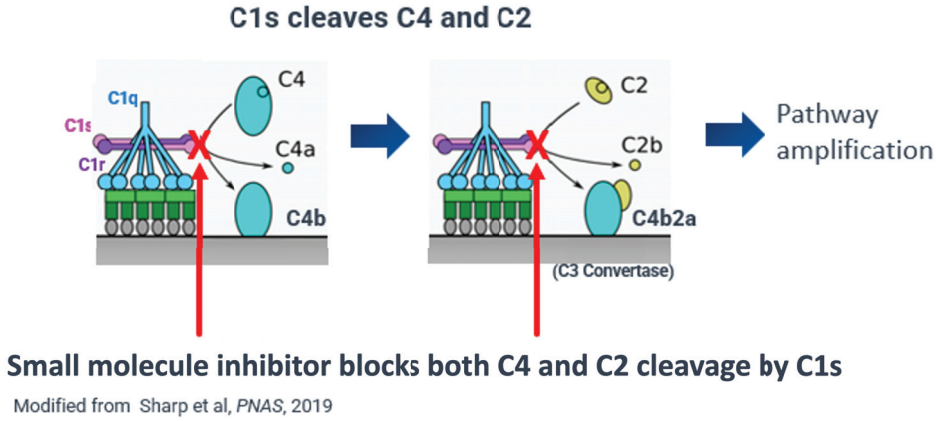
ANX1502

Overview of ANX1502

ANX1502 is a novel small molecule inhibitor of classical complement designed for oral administration in a range of chronic autoimmune diseases. ANX1502 converts to the active compound, ANX1439, on administration and delivers a highly potent and selective inhibitor of the activated form of C1s—part of the C1 complex that initiates the classical pathway. The active compound has been shown to have a high affinity to C1s and demonstrate a robust functional inhibition of the classical pathway.

Role of C1s in Complement-Mediated Autoimmune Diseases

The C1 complex is responsible for the activation of the classical pathway and is comprised of C1r, C1s and C1q. As part of the disease process, once activated, C1s is responsible for cleaving C4 and C2, key amplification components of the classical cascade. We believe that by stopping C1s from cleaving C4 and C2 with ANX1502, we will be able to block the classical cascade to reduce levels of inflammation, slow disease progression and potentially impact disease outcomes for patients.



Phase 1 SAD/MAD Trial of ANX1502

We completed the randomized, double-blind, placebo-controlled Phase 1 SAD/MAD trial of ANX1502 to assess the safety, tolerability, PK and PD of ANX1502 liquid suspension formulation in healthy adults. The study evaluated single ascending doses of ANX1502 ranging from 25 mg to 1050 mg (6 patients treated with ANX1502 plus 2 placebo subjects per cohort) and multiple ascending doses of ANX1502 ranging from 200 mg twice-daily to 525 mg twice-daily (9 patients treated with ANX1502 plus 3 placebo subjects per cohort).

In the SAD/MAD study, dose-proportional PK and targeted levels of active drug were observed across both cohorts, and single doses of 525-1025 mg ANX1502 suppressed C4d serum levels in healthy volunteers with higher than median baseline C4d. Across all doses evaluated, ANX1502 was generally well tolerated with mild to moderate treatment-emergent adverse events (TEAEs), which included gastro-intestinal events such as nausea, emesis and diarrhea. No serious adverse events were reported, and there were no significant clinical or lab findings.

Ongoing Development of ANX1502 in Autoimmune Diseases

We are evaluating a tablet formation of ANX1502 in an ongoing open-label, single arm POC study in patients with CAD for up to four weeks to assess tolerability, pharmacokinetics, pharmacodynamic and clinical efficacy endpoints (e.g., hemolysis as measured by reduction of elevated bilirubin). Enteric coated tablets allow flexible dosing 4-5-times above target concentrations of 100nM for rigorous testing in CAD, a classical complement-mediated disease. Three patients have been enrolled to date with observed reduction in key clinical and biomarker outcomes consistent with complement inhibition. Data in up to seven patients are expected in mid-2025.

Following the successful completion of the proof-of-concept study, we intend to evaluate ANX1502 in serious complement-mediated diseases, with the aim of providing enhanced efficacy and offering convenient dosing administration for long-term treatment of chronic autoimmune conditions.

Our Next Wave Programs

ANX005 for Huntington's Disease

We completed a Phase 2 trial of ANX005 in patients with HD (28 patients were enrolled with safety data measured from all 28 patients and efficacy data measured from 23 patients that completed both six-months of treatment and subsequent three-month follow-up period), which showed that treatment with ANX005 was generally well-tolerated, with full target engagement of C1q in both serum and CSF observed throughout the six-month treatment period and well into the three-month follow-up period. Disease progression stabilized for the entire nine months of the study, as assessed by both Composite Unified Huntington's Disease Rating Scale, or cUHDRS, and Total Functional Capacity, or TFC, the two primary clinical measurement scales for HD. Additionally, HD patients with higher baseline complement activity, as measured by elevated levels of C4a/C4 in CSF, demonstrated a rapid clinical benefit as early as week 6, as assessed by both cUHDRS and TFC, that was sustained over the entire nine months of the study. Plasma and CSF NfL levels remained generally consistent through the nine-month study and were comparable to NfL levels described in published natural history data for HD patients. Based on these findings and productive engagement with the FDA, we are assessing opportunities for late-stage development of ANX005 in HD.

ANX005 for ALS

We completed a Phase 2a signal-finding trial evaluating ANX005 in patients with ALS, designed to assess safety, tolerability, and target engagement (13 patients were enrolled and treated for 12 weeks, of which 7 patients continued on treatment for 24 weeks). Chronic dosing of ANX005 was generally well-tolerated, showed rapid and sustained target engagement of C1q in blood, and reduced downstream pharmacodynamic complement markers in blood. Consistent with what has been shown in other neurodegenerative diseases, including HD, exploratory analyses indicated that patients with higher baseline classical complement activation who enrolled within 12 months of diagnosis achieved better outcomes, including less functional decline on the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) and stabilization of neurofilament light chain (NfL). These analyses support a precision medicine approach to identify patients most likely to respond to anti-C1q therapy in clinical trials with recently diagnosed ALS patients who have elevated baseline levels of classical complement activity.

ANX009 for Lupus Nephritis

ANX009, an investigational C1q Fab formulated for subcutaneous delivery, which was most recently evaluated in a Phase 1b signal-finding trial using a precision medicine approach for patients with lupus nephritis (LN) who have high baseline complement activity. LN is an autoimmune disease for which pathogenic anti-C1q antibodies (PACAs) enhance activity and uniquely amplify kidney inflammation and damage. We designed ANX009 with a goal of enabling chronic dosing for patients with antibody-mediated autoimmune disorders where anti-C1q may have a disease-modifying effect and where we can utilize our targeted biomarker-driven approach. In a first-in-human clinical trial, ANX009 was well-tolerated (7 patients were enrolled, of which 6 patients completed treatment) at all dose levels tested and no drug-related safety signals were observed. The trial showed that ANX009 led to sustained C1q inhibition at multiple doses, supporting the potential for twice-weekly subcutaneous administration with the current formulation, and advancement into the Phase 1b signal-finding trial for patients with LN.

Initial results from the Phase 1b trial were presented at the American Society of Nephrology's Kidney Week 2023 conference, which showed subcutaneous ANX009 was well tolerated and demonstrated plasma C1q target engagement and complement inhibition. Importantly, inhibition of C1q rapidly increased free/circulating PACA levels (consistent with decreased deposition in the kidney) and improved all downstream markers of complement consumption and activation (C4, as well as C3 and C5b-9). These results indicate that C1q and the classical pathway are key drivers of complement activation in LN, independent of the alternative and lectin pathways, and that PACAs are a component of the classical complement activation pathway. Consistent with the short duration of this signal-finding study (3 weeks), changes in urinary protein excretion were not observed as anticipated. We are evaluating options for future development of ANX009 in LN.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, new therapeutic approaches and potential indications, and other inventions that are important to our business. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important for the development and implementation of our business. We also rely on the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how that is not patentable, we rely on confidentiality agreements to protect our interests. We generally require our employees, consultants, scientific advisors and contractors to enter into confidentiality agreements prohibiting the disclosure of confidential information and requiring disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Our patent portfolio includes patents and patent applications that are licensed to us in whole or in part from a number of partners, including Stanford University and the University of California, and patents and patent applications that are owned by us. Our proprietary technology has been primarily developed by in-house research and development programs, and to a lesser extent through acquisitions, relationships with academic research centers and contract research organizations.

For our product candidates, we will, in general, initially pursue patent protection covering compositions of matter and methods of use. Throughout the development of our product candidates, we seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including by protecting inventions related to additional methods of use, processes of making, formulation and dosing regimens.

We hold worldwide development and commercialization rights, including through exclusive licenses, to all of our product candidates, which allows us to strategically maximize value from our product portfolio over time. Our patent portfolio includes patent protection for our upstream complement platform and each of our product candidates.

As of February 10, 2025, our patent portfolio, including patents licensed from our partners, comprised 18 different patent families filed in various jurisdictions worldwide. Our patent portfolio includes issued patents and patent applications in the United States and in other jurisdictions.

One patent family, which we exclusively license from Stanford University, includes nine granted U.S. patents covering various methods of treating neurodegeneration and related medical conditions by inhibiting the C1 complex or its components, such as by using an anti-C1q antibody. The U.S. patents in this family include claims covering uses of ANX005, ANX007 and ANX009. These U.S. patents will expire between 2026 and 2030, absent any additional disclaimers, extensions or adjustments of patent term. There are no pending applications or foreign patents in this family.

Two other patent families, which we own, are directed to anti-C1q antibodies and methods of using them. These families include six granted U.S. patents, two pending U.S. patent applications, 30 granted foreign patents and eight pending foreign patent applications. The patents in these families cover ANX005, ANX007 and ANX009. These patents will expire between 2034 and 2037, absent any additional disclaimers, extensions or adjustments of patent term.

Other patent families that we own include:

- two granted U.S. patents, one pending U.S. patent application, eight granted foreign patents, and nine pending foreign patent applications. The patents in this family include claims directed to ANX007 and will expire between 2036 and 2038, absent any additional disclaimers, extensions or adjustments of patent term;
- one pending PCT application. The pending PCT application in this family includes claims covering a pharmaceutical formulation comprising anti-C1q antibodies, including ANX005, ANX007 and ANX009. Patents that may be issued from this family would expire in 2043, absent any disclaimers, extensions or adjustments of patent term;
- one granted U.S. patent, one pending U.S. patent application, and 37 pending foreign patent applications. The granted U.S. patent in this family includes claims covering certain small molecule modulators of the classical pathway, including ANX1502. This patent will expire in 2041, absent any additional disclaimers, extensions or adjustments of patent term. Patents that may be issued from these applications would expire in 2041, absent any disclaimers, extensions or adjustments of patent term; and
- one pending U.S. patent application and 16 pending foreign applications. The pending U.S. patent application in this family includes claims covering certain small molecule modulators of the classical pathway. Patents that may be issued from this family would expire in 2043, absent any disclaimers, extensions or adjustments of patent term.

Our patent portfolio also includes ten patent families, owned by us solely or jointly with the University of California or The J. David Gladstone Institutes or Fondazione Telethon and Universita' degli Studi di Trento, directed to the treatment of certain medical conditions using anti-C1q antibodies, including ANX005, ANX007 and ANX009. These families include nine pending U.S. patent applications, three granted foreign patents, and 84 pending foreign patent applications. Patents that may be issued from these applications would expire between 2034 and 2043, absent any disclaimers, extensions or adjustments of patent term.

Exclusive (Equity) Agreement with The Board of Trustees of the Leland Stanford Junior University

In November 2011, we and The Board of Trustees of the Leland Stanford Junior University, or Stanford, entered into an exclusive licensing agreement, or the Stanford Agreement. Under the Stanford Agreement, Stanford granted to us an exclusive, worldwide, royalty-bearing, sublicensable license, under certain patent rights, or the Licensed Patents, to make, use, offer for sale, sell, import and otherwise commercialize products covered by the Licensed Patents for human or animal diseases, disorders or conditions. We are required to meet certain development and funding milestones for the licensed products.

Under the Stanford Agreement, we are obligated to pay Stanford an upfront payment, license maintenance fees ranging from the single digit to tens of thousands of dollars per year, and milestone payments totaling up to $675,000. We also agreed to make royalty payments at a rate equal to a low single-digit percentage of worldwide net sales of licensed products and a portion of certain sublicensing income we receive from sublicensees at a rate in the low double digit percentages, subject to a specified maximum total payment.

Additionally, in accordance with the terms of the Stanford Agreement, upon closing our first financing event that raised at least $2.0 million, we granted Stanford $150,000 in shares of our redeemable convertible preferred stock, which were automatically converted into shares of our common stock prior to the completion of the initial public offering, or IPO, in July 2020. We may also have to pay a fee to Stanford if we assign our rights under the Stanford Agreement to a third party.

We may terminate the Stanford Agreement in its entirety, or as to a particular Licensed Patent or licensed product, for convenience on thirty days' prior written notice. Stanford may terminate the Stanford Agreement for our breach that remains uncured for forty-five days or if we provide any false report, are delinquent on any report or payment, fail to achieve a milestone or fail to diligently develop and commercialize a licensed product.

Patent Term and Term Extensions

Generally, utility patents issued for applications filed in the United States are granted a term of 20 years from the filing date of the earliest non-provisional patent application to which a claim of priority is made. In addition, in certain instances, the term of a U.S. patent can be extended to recapture a portion of any delay caused by the United States Patent and Trademark Office, or USPTO, in issuing the patent, as well as a portion of the term of a granted patent that is effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the restoration period cannot extend the patent term beyond 14 years from FDA approval for the product covered by that patent. In addition, only one patent applicable to an approved drug may receive the extension, and the extension applies only to coverage for the approved drug, methods for using it and methods of manufacturing it, even if the claims cover other products or product candidates. Where one patent covers multiple products or product candidates, it may only receive an extension for one of the covered products; any extension related to a second product or product candidate must be applied to a different patent. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from filing date of the earliest non-provisional patent application to which a claim of priority is made, such as a PCT application. All taxes, annuities or maintenance fees for a patent, as required by the USPTO and various foreign jurisdictions, must be timely paid in order for the patent to remain in force during this period of time.

The actual protection afforded by a patent may vary on a product by product basis, from country to country, and can depend upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions and the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Our patents and patent applications may be subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

Trademarks and Know-How

In connection with the ongoing development and advancement of our products and services in the United States and various international jurisdictions, we seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate.

In addition to patent and trademark protection, we rely upon know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by using confidentiality agreements with our commercial partners, collaborators, employees and consultants, and invention assignment agreements with our employees and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed by our employees and through relationships with third parties. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors, commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the

rights in related or resulting know-how and inventions. For more information, see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

Sales and Marketing

We hold worldwide commercialization rights, including through exclusive licenses, to our product candidates. Given our stage of development, we have established a small commercial organization and have not established distribution capabilities. Should any of our product candidates be approved for commercialization, we intend to develop a plan to commercialize them in the United States and other key markets, through internal infrastructure and/or external partnerships in a manner that will enable us to realize the full commercial value of our programs.

Manufacturing

Our success as a company will depend on our ability to deliver reliable, high-quality drug supply. We do not currently own or operate facilities for product manufacturing, storage and distribution, or testing. We contract with third parties for the manufacture of our product candidates. Because we rely on contract manufacturers, we employ personnel with extensive technical, manufacturing, analytical and quality experience. Our staff has strong project management discipline to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions.

Manufacturing is subject to extensive regulation that imposes various procedural and documentation requirements and that governs record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, and more. Our systems and our contractors are required to be in compliance with these regulations, and compliance is assessed regularly through monitoring of performance and a formal audit program.

Our current supply chains for our lead drug candidates involve several manufacturers that specialize in specific operations of the manufacturing process, specifically, raw materials procuring, drug substance manufacturing and drug product manufacturing. We currently operate under work order programs for our drug candidates with Master Services and Quality agreements in place that include specific supply timelines, volume and quality specifications. We are in discussions with our current manufacturers regarding preparation of Biologics License Applications (BLA) and Marketing Authorization Application (MAA) in the near future. This involves technology transfers, process characterization, and process validation to establish commercial manufacturing capabilities.

We intend to establish long-term supply agreements in the future. We believe our current manufacturers have the scale, the system, and the experience to supply our currently planned clinical trials and commercial launch. To ensure continuity in our supply chain, we plan to establish supply arrangements with alternative larger scale suppliers for certain portions of our supply chain, as appropriate.

Competition

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

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, and experience in obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Guillain-Barré Syndrome

There are currently no approved therapies for GBS in the United States. IVIg and PE are the most commonly used therapies in the Western world and parts of Asia. Currently, two investigational products are in development. Hansa Biopharma AB is conducting an open label Phase 2 trial of imlifidase in GBS patients in Europe and the United Kingdom for which it released topline results in December 2023 and real-world comparison data in December 2024. AstraZeneca/Alexion completed a Phase 3 trial of SOLIRIS (eculizumab) in Japan that did not meet its primary endpoint. Additionally, a primary investigator sponsored Phase 2 trial with argenx's efgartigimod is listed as an active trial.

Geographic Atrophy

Two treatments are currently FDA-approved for GA, both receiving approval in 2023: Apellis's Syfovre, a C3 inhibitor as well as Astellas's avacincaptad pegol, a C5 inhibitor. There are currently no approved therapies for GA in the EU. There is currently one combination complement cascade-targeted therapy in Phase 3 development for GA: Regeneron's pozelimab, a C5 inhibiting monoclonal antibody combined with cemdisiran, a C5-targeted siRNA molecule. In Phase 2, there are currently four complement-targeting agents: Aviceda Therapeutics's AVD-104, a nanoparticle molecule that inhibits complement cascade amplification and inflammation pathways, AstraZeneca's danicopan, an oral, complement factor D inhibitor, Janssen's JNJ 1887, a gene therapy candidate which expresses soluble CD59, a complement protein, and Novartis's iptacopan, an oral factor B inhibitor. Other products that do not target the complement cascade currently in Phase 2 or 3 clinical trials are being developed by Roche, Alkeus, Belite Bio, Stealth BioTherapeutics, Boehringer Ingelheim, Galimedix Therapeutics, Cognition Therapeutics and ONL Therapeutics. Perceive Bio, Ocugen, and Astellas each have an asset in Phase 1 of development.

Cold Agglutinin Disease, a type of autoimmune hemolytic anemia

Sanofi's Enjaymo was approved by the FDA for CAD in February 2022, and in October 2024, Sanofi sold global rights to Enjaymo to Italy-based Recordati. There are currently two investigational agents in clinical trials for CAD: Alpine Immune Sciences, Inc. is developing povetacicept, a fusion protein that blocks the function of two cytokines and Sanofi completed a phase I trial of BIVV020 in November 2023 with positive results with a single dose delivery in CAD patients.

Multifocal Motor Neuropathy

Currently, Gammagard Liquid (10% Immune Globulin Infusion (Human)) is the only therapy approved by the FDA for MMN. There are currently two agents in Phase 3 of development: Argenx's empasiprubart (ARGX-117), an IV-delivered C2 inhibitor and Takeda's TAK-771, which is being studied in a Japan-based Phase 3 trial. TAK-771 is a 10% Immune Globulin and Recombinant Human Hyaluronidase (rHuPH20) delivered as a subcutaneous infusion. There is also a complement-targeted agent, in Phase 2 development, Dianthus Therapeutics' DNTH103, a monoclonal antibody inhibitor of C1s.

Lupus Nephritis

There are currently two approved medicines specifically for LN: GSK's Benlysta and Aurinia's Lupkynis. One agent, Roche's obinutuzumab (Gazyva), has been filed with the FDA and EMA with approvals expected in 2025. There are four agents in development targeting the complement pathway, three in Phase 2 development and one in Phase 1 development: AstraZeneca's ravulizumab, a C5 inhibitor, vemircopan **(**ALXN2050), an oral Factor D inhibitor, and Novartis's iptacopan, an oral factor B inhibitor, are in Phase 2. AstraZeneca has a 3rd generation, subcutaneously administered C5 inhibitor, gefurulimab, which is being studied in a Phase 1, specifically for proteinuria. Outside of the complement pathway, there are currently four agents in Phase 3 development for adults with lupus: Novartis's ianalumab, AstraZeneca's anifrolumab, Vera Therapeutics's atacicept and Aurinia's voclosporin in adolescents with lupus nephritis. There are twelve cellular therapies in Phase 1 and Phase 1/2 of development as well as oral agents and monoclonal antibodies from BMS, Boehringer Engelheim, argenx, Janssen, Novartis and others in Phase 1 and Phase 2 development.

Huntington's Disease

There are no approved disease-modifying therapies for HD, and no potentially disease modifying agents in Phase 3 development. Multiple companies are developing potentially disease-modifying therapies in earlier stages of development, including, PTC Therapeutics's oral PTC518 in Phase 2, uniQure's gene therapy candidate, AMT-130 in Phase 1/2, Roche's tominersen in prodromal or early manifest HD patients aged 25-50 in Phase 2 and Vaccinex's pepinemab in Phase 2. Additional early-stage products in development are Wave Life Sciences's WVE-003 in Phase 1/2, Vico Therapeutics's V0659 in Phase 1/2 and Alnylam's ALN-HTT02 in Phase 1.

Amyotrophic Lateral Sclerosis

There are currently no additional complement-targeted therapies in clinical development. The drugs riluzole, Radicava and Radicava ORS (edaravone) are currently approved for the treatment of ALS and have shown modest effects in slowing the progression of the disease. Biogen's Qalsody, an antisense oligonucleotide that binds to SOD1 mRNA, for those ALS patients with SOD1-ALS, received accelerated approval from the FDA in April 2023. Amylyx's Relyvrio (AMX0035) was approved by the FDA in September 2022 for people living with ALS but was voluntarily pulled from the market by Amylyx after their Phase 3 confirmatory failed to show a benefit for ALS patients. Seven investigational agents are currently in Phase 3 development. There are a significant number of companies conducting earlier-stage clinical trials in ALS patients, including Ionis, argenx, Novartis, uniQure, NeuroSense, and others, testing oral agents, cellular therapies, gene therapies and other modalities.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of product candidates such as those we are developing. A new drug must be approved by the FDA through the approval process and a new biologic must be approved by the FDA through the biologics license application, or BLA, process before it may be legally marketed in the United States. We, along with third-party contractors, will be required to navigate the various preclinical, clinical manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biologics Regulation

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act, or FDCA, and in the case of biologics, also under the Public Health Service Act, or PHSA, and their implementing regulations. The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements, or GLP requirements and other applicable regulations;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before clinical trials may begin;
- approval by an institutional review board, or IRB, or ethics committee, or EC, at each clinical site before the trial is commenced at such site;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, requirements to establish the safety and efficacy of the proposed drug, or the safety, purity and potency of the proposed biologic for its intended purpose;
- preparation of and submission to the FDA of an NDA or BLA after completion of all required clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;

- a determination by the FDA within 60 days of its receipt of an NDA or BLA whether to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed drug or biologic is produced to assess compliance with current Good Manufacturing Practices, or cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of the BLA or NDA to permit commercial marketing of the product for specific indication(s) for use in the United States.

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Prior to beginning the first clinical trial with a product candidate in the United States, a sponsor must submit an IND to the FDA, which is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for the proposed clinical trial(s). The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically goes into effect 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

Furthermore, an independent IRB or EC for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the trial until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a Data Safety Monitoring Board, which provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Regulatory authorities, the IRB/ethics committee or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objective(s). There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

For purposes of BLA or NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These trials are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 trials may also be made a condition to approval of the BLA or NDA.

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

FDA Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA or NDA requesting approval to market the product candidate for one or more indications. The BLA or NDA must include all relevant data available from preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of the product candidate or from a number of alternative sources, including studies and trials initiated by investigators. The submission of a BLA or NDA requires payment of a substantial user fee to the FDA, and the sponsor of an approved BLA or NDA is also subject to an annual program fee. A waiver of user fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on BLAs or NDAs for products designated as Orphan Drugs, unless the application also seeks a non-orphan-designated indication.

Within 60 days following submission of the application, the FDA reviews a BLA or NDA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA or NDA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the Sponsor may meet with the FDA to confirm the additional information required to resubmit the BLA or NDA. Once a BLA or NDA has been accepted for filing, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after it accepts the application for filing. Priority review designation will direct overall attention and resources to the evaluation of applications for products that, if approved, would represent significant improvements in the safety or effectiveness of the treatment, diagnosis or prevention of serious conditions. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. 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. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facilities in which it is manufactured, processed, packed or held meet standards designed to assure the product's continued safety, purity and potency. The FDA may also convene a public Advisory Committee to provide additional expert insight on application review questions. The FDA is not bound by recommendations of an Advisory Committee, but it considers such recommendations when making decisions regarding approval.

Before approving a BLA or NDA, the FDA will typically inspect the facility or facilities where the product candidate 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 candidate within required specifications. Additionally, before approving a BLA or NDA, the FDA will typically inspect one or more clinical sites and/or the sponsor to assure compliance with GCP.

After the FDA evaluates a BLA or NDA and conducts inspections of clinical trial sites and manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an Approval Letter or a Complete Response Letter. An Approval Letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the BLA or NDA is not ready for approval in its present form and ends the current review cycle, and will describe all of the deficiencies that the FDA has identified in the BLA or NDA. The FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the BLA or NDA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA or NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. Additionally, the FDA may approve a BLA or NDA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Once approved, the FDA may withdraw the product approval if compliance with pre- and post- marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-marketing studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

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 product candidates that meet certain criteria. Specifically, drugs and biologics s 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. For a Fast Track product candidate, the FDA may consider sections of the BLA or NDA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the application. A BLA or NDA for a Fast Track-designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA or NDA at six months after the FDA accepts the application for filing. Priority review is granted when there is evidence that the product candidate, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious disease or condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior reviewers at FDA.

In addition, a product candidate may be eligible for accelerated approval. Drugs and biologics intended to treat serious or life threatening diseases or conditions may be eligible for accelerated approval upon a determination that the drug or biologic has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or 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 generally requires sponsors of products receiving accelerated approval to conduct well-controlled confirmatory required to verify or characterize the drug or biologic's predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The FDA may withdraw approval of a product or indication approved under accelerated approval if, for example, the sponsor fails to conduct any required confirmatory studies in a timely manner, or if such studies fail to verify the predicted clinical benefit of the product.

Fast Track designation, priority review, accelerated approval 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.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant Orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan Drug designation must be requested before submitting a BLA or NDA. After the FDA grants Orphan Drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval requirements or process.

If a product candidate that has Orphan Drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA or NDA, to market the same biologic or chemical entity for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with Orphan Drug exclusivity or if the FDA finds that the holder of the Orphan Drug exclusivity has not shown that it can assure the availability of sufficient quantities of the Orphan Drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan Drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of Orphan Drug designation are tax credits for certain research and development activities and a waiver of the BLA or NDA application user fee.

A designated Orphan Drug may not receive Orphan Drug exclusivity if it is approved for a use that is broader than the indication for which it received Orphan designation. In addition, Orphan Drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with Orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Any drugs or biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug and biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state

agencies for compliance with cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, Warning Letters, or untitled enforcement letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drugs and biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of so-called "off-label" uses. Failure to comply with these requirements can result in, among other things, adverse publicity, Warning Letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, signed into law in 2010, includes a subtitle called the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to, or interchangeable with, an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the

reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Drug Product Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. For example, the FDCA provides a five-year period of non-patent data exclusivity within the United States 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 any 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 United States. 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, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Other Healthcare Laws and Compliance Requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal and state fraud and abuse laws, including false claims, civil monetary penalties, consumer protection and transparency laws regarding drug pricing and payments or other transfers of value made to physicians and other licensed healthcare professionals, as well as similar foreign laws in the jurisdictions outside the United States. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, additional reporting obligations, contractual damages, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations, and standards govern the collection, use, access to, confidentiality and security of health-related and other personal data, including clinical trial data, and apply now or could apply in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal data. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. For example, the European Union General Data Protection Regulation, or the EU GDPR, imposes strict requirements for processing the personal data of individuals within the European Economic Area, or the EEA. Companies that must comply with the EU GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Further, from January 1, 2021, certain companies that have had to comply with the EU GDPR also have to comply with the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. Privacy and security laws, regulations, and other obligations globally are evolving, may conflict with each other (which complicate compliance efforts and increases compliance cost), and can result in investigations, proceedings, and other actions that can lead to significant civil and/or criminal penalties and fines.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. No uniform policy exists for coverage and reimbursement for products exists among U.S. third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. The process for determining whether a third-party payor will provide coverage for a product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost-sharing obligation imposed on patients. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our product candidates to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. Furthermore, there can be no assurance that a product will be considered medically reasonable and necessary for a specific indication, that a product will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payor's reimbursement policies will not adversely affect the ability to sell a product profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the ACA was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States and significantly affected the pharmaceutical industry. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and fraud and abuse changes. Additionally, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70.0% 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; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs; implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; expanded eligibility criteria for Medicaid programs; 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; and established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been amendments to and judicial, Congressional and executive branch challenges to certain aspects of the ACA. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted, including aggregate reductions of Medicare payments to providers, which will remain in effect through 2032, absent additional Congressional action. In addition, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100.0% of a drug's average manufacturer price, effective January 1, 2024.

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 legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. Most recently, the IRA, among other things, (1) directs the U.S. Department of Health and Human Services, or HHS, to negotiate the price of certain single-source drugs and biologics that have been on the market for at least 7 years covered under Medicare, or Medicare Drug Price Negotiation Program, and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions began to take effect beginning fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon price of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. The IRA permits the Secretary of the Department of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. Individual states in the United States have also become increasingly active in implementing 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, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare product candidates and services, which could result in reduced demand for our product candidates once approved or additional pricing pressures.

Human Capital Resources

As of December 31, 2024, we had 100 full-time employees, 80 of whom were primarily engaged in research and development activities. A total of 38 employees have an M.D., Ph.D. or Pharm.D. degree. Most of our employees are based in our Brisbane, California facility, subject to hybrid and remote work arrangements.

We believe that our future success will depend, in part, on our ability to continue to attract, hire, and retain qualified personnel. We continue to seek additions to our science and technical staff. Through our experience with technological innovation, we appreciate the importance of retention, growth and development of our employees. We believe we offer competitive compensation (including salary, incentive bonus, and equity) and benefits packages. None of our employees is represented by a labor union, and we consider our employee relations to be good.

Corporate Information

We were incorporated under the laws of the State of Delaware on March 3, 2011. Our principal executive offices are located at 1400 Sierra Point Parkway, Bldg C, Suite 200, Brisbane, California 94005, and our telephone number is (650) 822-5500. Our corporate website address is www.annexonbio.com. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this Annual Report on Form 10-K.

Available Information

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements, and related amendments, exhibits and other information with the Securities and Exchange Commission, or the SEC. You may access and read our filings without charge through the SEC's website at www.sec.gov or through our website at https://ir.annexonbio.com/financial-information/sec-filings, as soon as reasonably practicable after such materials are electronically filed with or furnished to the SEC pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this Annual Report on Form 10-K.

Item 1A. Risk Factors.

Our business involves significant risks, some of which are described below. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and the related notes. If any of the following risks actually occur, it could harm our business, prospects, results of operations and financial condition and future prospects. In such event, the market price of our common stock could decline and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

We are a clinical-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability.

We are a clinical-stage biopharmaceutical company, and we have only a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have no products approved for commercial sale and have not generated any revenue from sales of our product candidates and have incurred losses in each year since our inception in March 2011. We have only a limited operating history upon which you can evaluate our business and prospects. In addition, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical, biopharmaceutical and biotechnology industry.

We have had significant operating losses since our inception. Our net loss for the years ended December 31, 2024 and 2023 was approximately $138.2 million and $134.2 million, respectively. As of December 31, 2024, we had an accumulated deficit of $710.7 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will continue as we develop our product candidates, conduct clinical trials and pursue research and development activities. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We will require substantial additional financing to achieve our goals, 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 programs, commercialization efforts or other operations.

Since our inception, we have invested a significant portion of our efforts and financial resources in research and development activities. Our product candidates will require additional clinical development, and we intend to conduct additional research and development activities to discover and develop new product candidates, including conducting preclinical studies and clinical trials, all of which will require substantial additional funds. We will continue to expend significant resources for the foreseeable future in connection with these activities. These expenditures will include costs associated with conducting preclinical studies and clinical trials, obtaining regulatory approvals and manufacturing and supply, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any preclinical study or clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or any future product candidates.

As of December 31, 2024, we had capital resources consisting of cash and cash equivalents and short-term investments of approximately $312.0 million. We expect our existing capital resources to fund our planned operating expenses into the second half of 2026. However, our operating plans may change as a result of many factors currently

unknown to us, and we may need to seek additional funds sooner than planned through public or private equity offerings or debt financings or other sources, such as strategic collaborations. Such financing may result in dilution to our stockholders, imposition of burdensome debt covenants and repayment obligations, or other restrictions that may affect our business. 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 future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our current product candidates or any other future product candidates we choose to pursue, conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining feedback from regulators on our clinical trials and regulatory approvals for our product candidates or any future product candidates;
- the number and characteristics of any additional product candidates we develop or acquire;
- the timing and amount of any milestone, royalty and/or other payments we are required to make pursuant to our current or any future license or collaboration agreements;
- the cost of manufacturing our product candidates or any future product candidates and any products we successfully commercialize;
- the cost of building a sales force in anticipation of product commercialization;
- the cost of commercialization activities of our product candidates, if approved for sale, including marketing, sales and distribution costs;
- our ability to establish strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract, hire and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio; and
- the timing, receipt and amount of sales of any future approved products.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, macroeconomic factors, including recent and potential bank failures, increasing inflation and interest rates, exchange rate fluctuations and supply chain disruptions, geopolitical conflicts, such as the war in Ukraine and hostilities in the Middle East, and disruptions to and volatility in the credit and financial markets in the United States and worldwide. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for our product candidates or any future product candidate;
- delay, limit, reduce or terminate our research and development activities; or
- delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates or any future product candidate or reduce our flexibility in developing or maintaining our sales and marketing strategy.

We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue on our own. We do not expect to realize revenue from sales of products or royalties from licensed products in the foreseeable future, if at all, and unless and until our product candidates are clinically tested, approved for commercialization and

successfully marketed. To date, we have primarily financed our operations through the sale of equity securities and warrants to purchase our equity securities. We will be required to seek additional funding in the future and currently intend to do so through public or private equity offerings or debt financings, credit or loan facilities, collaborations or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

Due to the significant resources required for the development of our product candidates, we must prioritize development of certain product candidates and/or certain disease indications. We may expend our limited resources on candidates or indications that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We are currently focused on developing product candidates to address classical complement-mediated autoimmune and neurodegenerative diseases. We seek to maintain a process of prioritization and resource allocation among our programs to balance time, risk and cost, due to the significant resources required for the development of our product candidates. Our resources are currently focused on advancing ANX005 in GBS, ANX007 in GA and ANX1502 in autoimmune diseases. If sufficient funding is not available, we may not be able to complete our planned clinical trials, or on the timelines we currently anticipate, and we may need to redesign, reduce the scope of or terminate some of our programs.

Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, any decision to delay, terminate or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the autoimmune or neurodegenerative or pharmaceutical, biopharmaceutical or biotechnology industry, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain development and commercialization rights.

Conducting a global Phase 3 program for ANX007 in patients with dry AMD with GA will be expensive and time consuming, and we may need additional capital to complete the Phase 3 clinical program and even if favorable, the FDA and comparable foreign regulatory authorities may not accept data from our Phase 3 program.

Recent regulatory engagement regarding the Phase 3 ARCHER II trial design has established a global registration path for ANX007 in the U.S. and Europe. As a result, we are conducting ARCHER II, a global sham-controlled double-masked, Phase 3 trial. The single-study program will be analyzed as two sub-studies for the U.S. in accordance with the FDA's two-trial recommendation. The primary endpoint of ARCHER II is prevention of ≥15-letter loss of BCVA, and an objective secondary structural measure is prevention of EZ loss. Accordingly, Annexon no longer plans to conduct a second injection-controlled head-to-head Phase 3 trial. There can be no assurance that the FDA and comparable regulatory authorities will accept the data from our Phase 3 program or determine that it is sufficient to support approval.

Conducting large Phase 3 trials in multiple jurisdictions is expensive and can take many years to complete, and we cannot guarantee that clinical trials will be conducted as planned or completed timely, if at all. In addition, there are two FDA-approved therapies for GA in the United States, which may adversely impact our ability to recruit patients into our clinical trials. Our timeline and costs for ARCHER II could be substantially longer and larger than

we initially planned. We may need additional capital to complete the Phase 3 clinical program for ANX007 and may not be able to raise sufficient capital in a timely manner. The occurrence of any such events could delay either trial, prevent us from completing our clinical trials, prevent us from seeking FDA approval of ANX007, if ever, and could delay or prevent commercialization of ANX007.

Our results of operations may fluctuate significantly, which makes our future results of operations difficult to predict and could cause our results of operations to fall below expectations.

Our quarterly and annual results of operations may fluctuate significantly, which makes it difficult for us to predict our future results of operations. These fluctuations may occur due to a variety of factors, many of which are outside of our control and may be difficult to predict, including:

- the timing and cost of, and level of investment in, research, development and, if approved, commercialization activities relating to our product candidates, which may change from time to time;
- the timing and status of enrollment for our clinical trials;
- the cost of manufacturing our product candidates, as well as building out our supply chain, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;
- timing and amount of any milestone, royalty or other payments due under any collaboration or license agreement;
- future accounting pronouncements or changes in our accounting policies;
- the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- the timing of receipt of approvals for our product candidates from regulatory authorities in the United States and internationally;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our products; and
- the level of demand for our product candidates, if approved, which may vary significantly over time.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual results of operations. As a result, comparing our results of operations on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or results of operations fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if any forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Risks Related to Our Business

Our business is heavily dependent on the successful development, regulatory approval and commercialization of our product candidates, some of which are in early stages of clinical development.

We have no products approved for sale, and several of our product candidates are in early stages of clinical development. The success of our business, including our ability to finance our company and generate revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of our product candidates and, in particular, the advancement of our current clinical-stage product candidates. However,

given the stage of development of our product candidates, it may be many years, if we succeed at all, before we have demonstrated the safety, purity, potency and/or efficacy of a product candidate sufficient to warrant approval for commercialization. We cannot be certain that our product candidates will receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

While inhibition of the complement pathway has been validated as a therapeutic approach, C1q inhibition is a novel therapeutic approach, which exposes us to certain risks. For example, we may discover that our product candidates do not possess certain properties required for therapeutic effectiveness, or even if found to be effective in one type of disease, they are not effective in other types of disease. In addition, given the novel nature of this therapeutic approach, designing preclinical studies and clinical trials to demonstrate the effect of the product candidates is complex and exposes us to risks, including that our biomarker-driven approach may not translate into therapeutic effectiveness.

In the future, we may also become dependent on other product candidates that we may develop or acquire. The clinical and commercial success of our product candidates and future product candidates will depend on a number of factors, including the following:

- our ability to raise any additional required capital on acceptable terms, or at all;
- our ability to complete an investigational new drug application, or IND, enable studies and successfully submit INDs or comparable applications;
- timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- whether we are required by the U.S. Food and Drug Administration, or the FDA, or similar foreign regulatory agencies to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- acceptance of our proposed indications and primary endpoint assessments relating to the proposed indications of our product candidates by the FDA and similar foreign regulatory authorities;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, efficacy and acceptable risk to benefit profile of our product candidates or any future product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future approved products, if any;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain compliance with our contractual obligations and with all regulatory requirements applicable to our product candidates or any future product candidates or approved products, if any;
- the ability of third parties with whom we contract to manufacture adequate clinical trial and commercial supplies of our product candidates or any future product candidates remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMPs;
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- the convenience of our treatment or dosing regimen;

- acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidates or any future product candidates, if approved, including relative to alternative and competing treatments;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates or any future product candidates, if approved;
- patient demand for our product candidates, if approved, including the willingness of patients to pay out-of-pocket for any approved products in the absence of coverage and/or adequate reimbursement from third-party payors;
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates; and
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize our product candidates. Even if regulatory approvals are obtained, we may never be able to successfully commercialize any of our product candidates. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of our product candidates or any future product candidates to continue our business or achieve profitability.

Public health crises such as pandemics or similar outbreaks have, and could in the future, materially and adversely affect our preclinical and clinical trials, business, financial condition and results of operations.

As a result of public health crises, including the COVID-19 pandemic, we have experienced, and may in the future experience, disruptions that could materially and adversely impact our clinical trials, business, financial condition and results of operations. These disruptions include but are not limited to:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in initiating or expanding clinical trials, including delays or difficulties with clinical site initiation and recruiting clinical site investigators and clinical site staff;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of health conditions;
- interruption of key clinical trial activities, such as clinical trial site data monitoring and efficacy, safety and translational data collection, processing and analyses, due to limitations on travel imposed or recommended by federal, state or local governments, employers and others or interruption of clinical trial subject visits, which may impact the collection and integrity of subject data and clinical study endpoints;
- 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 our clinical trials;
- delays or disruptions in preclinical experiments and IND-enabling studies due to restrictions of on-site staff and unforeseen circumstances at contract research organizations, or CROs, and vendors;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- limitations on employee or other resources that would otherwise be focused on the conduct of our clinical trials and pre-clinical work, including because of sickness of employees or their families, the desire of employees to avoid travel or contact with large groups of people, an increased reliance on working from home, school closures or mass transit disruptions;

- changes in regulations as part of a response to pandemics or similar outbreaks, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel; and
- refusal of the FDA to accept data from clinical trials in affected geographies outside the United States.

The extent to which any future outbreak may affect our clinical trials, business, financial condition, results of operations and clinical development timelines and plans will depend on factors including the duration of the outbreak, rates of infection in the locations in which we and our CROs, third-party manufacturers, regulatory authorities and other third parties with whom we do business operate, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Future developments in these and other areas present material uncertainty and risk with respect to our clinical trials, business, financial condition and results of operations.

Research and development of biopharmaceutical products is inherently risky. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

We are at an early stage of clinical development of our product candidates. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for and successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If any of these events occur, we may be forced to abandon our development efforts for a product candidate or candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations. Failure of a product candidate may occur at any stage of preclinical or clinical development, and we may never succeed in developing marketable products or generating product revenue.

We may not be successful in our efforts to further develop our current and future product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates will require significant additional clinical development, management of preclinical, clinical and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization and significant marketing efforts before we generate any revenue from product sales, if at all. Any clinical studies that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future clinical studies are inconclusive with respect to the efficacy of our product candidates, if we do not meet the clinical endpoints with

statistical significance or if there are safety concerns or adverse events associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for our product candidates.

The FDA or other regulatory agencies may not agree with our clinical development plan and require that we conduct additional clinical trials to support our regulatory submissions. Regulatory agencies, including the FDA may require that we conduct more than one pivotal trial in order to gain approval.

Furthermore, clinical trials must be conducted in accordance with the laws, rules and regulations, guidelines and other requirements of the FDA, the European Medicines Agency, or the EMA, and other applicable regulatory authorities outside of those jurisdictions and are subject to oversight by these regulatory authorities and institutional review boards, or IRBs, or ethics committees at the medical institutions where such clinical trials are conducted. Further, conducting global clinical trials, as we do for GBS and GA, may require that we coordinate among the legal requirements and guidelines of regulatory authorities across a number of jurisdictions, including the United States, the European Union, or the EU, and countries outside of those jurisdictions, which could require that we amend clinical trial protocols or determine not to conduct a trial in one or more jurisdictions or to run separate trials in various jurisdictions due to the inability, cost or delay in harmonizing divergent requests from such regulatory authorities, all of which could increase costs. In addition, clinical trials that are conducted in countries outside the United States and the EU may subject us to risks associated with the engagement of non-United States and non-EU CROs who are unknown to the FDA or the EMA, or the EU member states' regulatory authorities and may have different standards of diagnosis, screening and medical care, as well as risks associated with further delays and expenses as a result of increased shipment costs (including as a result of local quality release or in-country testing of a product candidate supply produced in a different jurisdiction for our clinical trials) and political and economic risks relevant to such countries outside the United States and the EU.

If any of our product candidates successfully completes clinical trials, we plan to seek regulatory approval to market our product candidates in the United States, the European Union, or the EU, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing and distribution of our product candidates. We may also rely on collaborators or partners to conduct the required activities to support an application for regulatory approval and to seek approval for one or more of our product candidates. We cannot be sure that any such collaborators or partners will conduct these activities successfully or do so within the timeframe we desire. Even if we or any future collaborators or partners are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Any approval we may obtain could be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a Risk Evaluation and Mitigation Strategy, or REMS. The failure to obtain timely regulatory approval of product candidates, any product marketing limitations or a product withdrawal would negatively impact our business, results of operations and financial condition.

We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an IND or a clinical trial application, or CTA, will result in the FDA or other regulatory

authority, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- generating sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- delays in obtaining regulatory authorization to commence a trial;
- reaching agreements 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 trial sites;
- identifying, recruiting and training suitable clinical investigators;
- obtaining IRB approval at each trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, or equivalent foreign application or amendment;
- new safety findings that present unreasonable risk to clinical trial participants;
- a negative finding from an inspection of our clinical trial operations or study sites;
- recruiting an adequate number of suitable patients to participate in a trial;
- having subjects complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- addressing subject safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites; or
- obtaining sufficient product supply of product candidates for use in preclinical studies or clinical trials from third-party suppliers.

We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials or require that we submit additional data or information before allowing a clinical trial to be initiated;
- clinical studies of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls or be unable to provide us with sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;

- the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements and add new requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

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

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

For example, we intend to seek FDA approval of ANX005 for the treatment of patients with GBS. We are preparing for a pre-BLA meeting with FDA, targeted for the first half of 2025. Our data package is based on clinical trials conducted outside the United States and includes a placebo-controlled Phase 1b trial that established POC for ANX005 as a first-line treatment for GBS, a successful Phase 3 trial showing that ANX005 was generally well tolerated and resulted in faster and more complete functional recovery versus placebo, a RWE study that showed improved outcomes against current standards of care in matched patient populations, and a drug-drug interaction study with ANX005 and IVIg strengthening the safety profile for ANX005 in GBS. The FDA may not agree that this RWE data is sufficient to support generalizability of the Phase 3 results to a U.S. population. The FDA ordinarily requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the safety and efficacy of a biologic for approval, and our single Phase 3 trial may be inadequate. The FDA may not agree that the data package is sufficient to accept for filing a BLA, and we may receive a refusal to file letter and be required to conduct additional clinical trials of ANX005 for GBS prior to resubmission of a BLA, which would result in delays in our application process and increase our expenses, and delay or prevent commercialization of ANX005 in GBS. Even if accepted for filing by the FDA, any such BLA could be the subject of a complete response letter rather than approval, which would increase our expenses and delay or prevent commercialization of ANX005 in GBS.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial 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 drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries, as we plan to do for certain of our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural

customs and managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks.

Principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or a regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing our current or future product candidates.

If we experience delays in the completion, or termination, of any preclinical study or clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate revenues from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our clinical trials may increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may materially and adversely affect our business, financial condition, results of operations and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. If one or more of our product candidates proves to be ineffective, unsafe or commercially unviable, our business, financial condition, results of operations and prospects may be materially and adversely affected.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to initiate or continue clinical trials on a timely basis or at all for any product candidates we identify or develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. The timely completion of clinical trials in accordance with their protocols depends on, among other things, our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the severity and difficulty of diagnosing the disease under investigation;
- the patient eligibility and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the existing body of safety and efficacy data with respect to the study drug and safety concerns;
- patient referral practices of physicians;
- risk that enrolled subjects will drop out before completion of the trial, including as a result of health conditions or being forced to quarantine;
- ability to monitor patients adequately during and after treatment;
- availability and efficacy of approved medications or therapies, or other clinical trials, for the disease or condition under investigation;

- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating; and
- our ability to obtain and maintain patient consents.

In addition, our clinical trials may 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. In addition, patients may not opt to enroll in our trials because of the availability of approved therapeutics for their disease. Because the number of qualified clinical investigators is limited, we may 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 in such clinical trial site. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any of our product candidates could halt their clinical development, delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us or 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 comparable foreign regulatory authorities. We have experienced adverse events during clinical trials, and may in the future experience, adverse or unforeseen events during, or as a result of, clinical trials. If unacceptable side effects arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted or the DSMB could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may materially and adversely affect our business, financial condition, results of operations and prospects.

In addition, early clinical trials may only include a limited number of subjects and limited duration of exposure to our product candidates. In particular, we are pursuing a novel approach to inhibiting upstream molecules of the classical complement pathway, primarily C1q, and as a result, our product candidates may cause unforeseen safety events when evaluated in larger patient populations. Further, clinical trials may not be sufficient to determine the effect and safety consequences of taking our product candidates over a multi-year period.

If any of our product candidates receives marketing approval, and we or others later identify undesirable and unforeseen side effects caused by such product, a number of potentially significant negative consequences could result, including but not limited to:

- 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.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business. In addition, if one or more of our product candidates prove to be unsafe, our business, financial condition, results of operations and prospects may be materially and adversely affected.

Interim, "top-line" and preliminary data from studies or trials that we announce or publish from time to time may change as more 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 publicly disclose interim, "top-line" or preliminary data from preclinical studies or clinical trials. Interim data are subject to the risk that one or more of the outcomes may materially change as more data become available. 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 when we publish such data. As a result, the "top-line" results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. "Top-line" or preliminary 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" and preliminary data should be viewed with caution until the final data are available. From time to time, we also disclose interim data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim, "top-line" or preliminary data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the "top-line," preliminary or interim data that we report differ from final results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

Even if our current or future product candidates obtain regulatory approval, they may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success.

Even if one or more of our product candidates receive FDA or other regulatory approvals, the commercial success of any of our current or future product candidates will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. Our product candidates may not be commercially successful. For a variety of reasons, including, among other things, competitive factors, pricing or

physician preference, reimbursement by insurers, the degree and rate of physician and patient adoption of our current or future product candidates, if approved, will depend on a number of factors, including:

- the clinical indications for which the product is approved and patient demand for approved products that treat those indications;
- the safety and efficacy of our product as compared to other available therapies; for example, with respect to ANX007, physicians may prescribe or patients may prefer recently approved therapies for the treatment of GA;
- the availability of coverage and adequate reimbursement from managed care plans, insurers and other healthcare payors for any of our product candidates that may be approved;
- acceptance by physicians, operators of clinics and patients of the product as a safe and effective treatment;
- physician and patient willingness to adopt a new therapy over other available therapies to treat approved indications;
- overcoming any biases physicians or patients may have toward particular therapies for the treatment of approved indications;
- proper training and administration of our product candidates by physicians and medical staff;
- public misperception regarding the use of our therapies, if approved for commercial sale;
- patient satisfaction with the results and administration of our product candidates and overall treatment experience, including, for example, the convenience of any dosing regimen;
- the cost of treatment with our product candidates in relation to alternative treatments and reimbursement levels, if any, and willingness to pay for the product, if approved, on the part of insurance companies and other third-party payors, physicians and patients;
- the revenue and profitability that our products may offer a physician as compared to alternative therapies;
- the prevalence and severity of side effects;
- limitations or warnings contained in the FDA-approved labeling for our products;
- the willingness of physicians, operators of clinics and patients to utilize or adopt our products as a solution;
- any FDA requirement to undertake a REMS;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about our products or favorable publicity about competitive products; and
- potential product liability claims.

We cannot assure you that our current or future product candidates, if approved, will achieve broad market acceptance among physicians and patients. Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our results of operations.

We have received Orphan Drug designation for ANX005 for the treatment of GBS and HD in the United States and for GBS in Europe, and we may seek Orphan Drug designation for certain future product candidates. We may be unable to obtain such designations or to maintain the benefits associated with Orphan Drug designation, including market exclusivity, which may cause any revenue from product sales to be reduced.

We have received Orphan Drug designation in the United States for ANX005 for the treatment of GBS and HD and for the treatment of GBS in Europe from the European Medicines Agency, or EMA. Although we may seek Orphan product designation for some or all of our other product candidates, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a drug or biologic product as an Orphan Drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of

developing the drug will be recovered from sales in the United States. Orphan Drug designation must be requested before submitting a biologics license application, or BLA, or new drug application, or NDA. In the EU, the EMA's Committee for Orphan Medicinal Products, or COMP, 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 EU. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, Orphan Drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and application fee waivers. After the FDA grants Orphan Drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA.

In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to Orphan Drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same disease or condition for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with Orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity to the orphan patient population. Exclusive marketing rights in the United States may also be unavailable if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective. In the EU, Orphan Drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the Orphan Drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable to not justify maintenance of market exclusivity.

Even if we obtain Orphan Drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain Orphan Drug exclusivity for a product candidate, 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 can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is 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 or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process.

A Breakthrough Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

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

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In

addition, even if one or more of our product candidates qualify as breakthrough therapies, 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.

A Fast Track designation by the FDA or PRIME designation by the EMA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

The FDA has granted Fast Track designation for ANX005 in GBS and for ANX007 in GA, and the EMA has granted PRIME designation for ANX007 in GA, and, in the future, we may seek Fast Track designation or PRIME designation for our product candidates. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the drug or biologic demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for Fast Track designation. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA or NDA is submitted, the application may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA or 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 BLA or NDA, the FDA agrees to accept sections of the BLA or NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA or NDA. The FDA has broad discretion whether or not to grant this designation.

PRIME is a program launched by the EMA to enhance support for research on and development of medicines that have demonstrated preliminary safety and efficacy and thus the potential to target a significant unmet medical need and bring a major therapeutic advantage to patients. This regulatory program offers developers of promising medicines enhanced interaction and early dialogue with the EMA and is designed to optimize development plans and speed evaluation ensuring these medicines reach patients as early as possible. The EMA has broad discretion whether or not to grant this designation.

Even if we believe a particular product candidate is eligible for these designations, we cannot assure you that the FDA, EMA or similar regulatory agency would decide to grant them. Fast Track and PRIME designations may not result in a faster development process, review or approval compared to conventional FDA or EMA procedures, respectively. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. The Fast Track and PRIME designations do not assure ultimate regulatory approval by the FDA or the EMA. Many drugs and biologics that have received Fast Track or PRIME designation have failed to obtain approval.

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

The ability of the FDA to review and/or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies or comparable foreign regulatory authorities may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Similar considerations are applicable to foreign regulatory authorities.

If a prolonged government shutdown occurs, or if new or existing global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory

activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We conduct, and in the future plan to conduct, clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We conduct clinical trials of our product candidates outside the United States, and plan to continue to do so. For example, we conducted our Phase 1b GBS clinical trial of ANX005 in Bangladesh, and have completed our Phase 3 clinical trial of ANX005 in patients with GBS at sites in Bangladesh and the Philippines. We are also conducting a global Phase 3 program for ANX007 in dry AMD with GA. The acceptance of study data from clinical trials conducted outside the United States or the applicable jurisdiction by the FDA and comparable foreign regulatory authorities may be subject to certain conditions, or may not be accepted at all.

For example, where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, regardless of whether such trials were conducted under an IND, the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the United States population and United States medical practice, the trials were performed by clinical investigators of recognized competence and the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. For trials that are conducted only at sites outside of the United States and not subject to an IND, the FDA requires the clinical trial to have been conducted in accordance with good clinical practice, or GCP, requirements, and the FDA must be able to validate the data from the clinical trial through an on-site inspection if it deems such inspection necessary. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in product candidates that we may develop not receiving approval or clearance for commercialization in the applicable jurisdiction.

To support data from clinical trials conducted in foreign jurisdictions, applicants may submit clinical evidence, clinical trials, patient registries or other sources of RWE, such as electronic health records or the collection of larger confirmatory data sets. In particular, because all of our studies to date for ANX005 in GBS have been conducted at sites outside the United States, we have conducted a RWE study to assess comparability of disease populations in the US and ex-US using a large natural history database from IGOS. Published data from IGOS presents baseline characteristics of GBS patients in various jurisdictions and patient outcomes at certain timepoints over the course of their disease. We intend to use the results of the RWE study along with any other requested information for generalizability of Southeast Asian patients to a Western population as part of our data package in support of the ANX005 BLA. However, the FDA may not agree that the current data package is sufficient to accept for filing a BLA and we may receive a refusal to file letter and be required to conduct additional clinical trials of ANX005 for GBS prior to resubmission of a BLA, which would result in delays in our application process and increase our expenses, and delay or prevent commercialization of ANX005 in GBS. Even if accepted for filing by the FDA, any such BLA could be the subject of a complete response letter rather than approval, which would increase our expenses and delay or prevent commercialization of ANX005 in GBS.

In addition, we are conducting a global registrational program of ANX007 for the treatment of dry AMD with GA. To accomplish this objective, we must obtain and maintain regulatory approvals and comply with regulatory requirements in each jurisdiction. We are in ongoing discussions with the relevant regulatory authorities. While we believe we have designed a global clinical development program that could satisfy the regulators in all of our target markets, there is no assurance that our efforts will be successful or that the various regulators will be aligned or accept the data from the Phase 3 program are sufficient to warrant approval of ANX007.

If the product candidates that we develop receive regulatory approval in the United States or another jurisdiction, they may never receive approval in other jurisdictions, which would limit market opportunities for our product candidates and adversely affect our business.

Approval of a product candidate in the United States by the FDA or by the requisite regulatory agencies in any other jurisdiction does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions. The approval process varies among countries and may limit our or any future collaborators' ability to develop, manufacture, promote and sell product candidates internationally. Failure to obtain marketing approval in international jurisdictions would prevent the product candidates from being marketed outside of the jurisdictions in which regulatory approvals have been received. In order to market and sell product candidates in the EU, and many other jurisdictions, we and any future collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional preclinical studies or clinical trials both before and after approval. In many countries, any product candidate for human use must be approved for reimbursement before it can be approved for sale in that country. In some cases, the intended price for such product is also subject to approval. Further, while regulatory approval of a product candidate in one country does not ensure approval in any other country, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we or any future collaborators fail to comply with the regulatory requirements in international markets or to obtain all required marketing approvals, the target market for a particular potential product will be reduced, which would limit our ability to realize the full market potential for the product and adversely affect our business.

Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

We rely on third-party suppliers to manufacture our product candidates, and we intend to rely on third parties to produce commercial supplies of any approved product. The loss of these suppliers, or their failure to comply with applicable regulatory requirements or to provide us with sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.

We do not have the ability, and we do not plan to build or acquire the infrastructure or capability internally, to manufacture supplies of our product candidates or the materials necessary to produce our product candidates for use in the conduct of our preclinical studies or clinical trials, and we lack the internal resources and the capability to manufacture any of our product candidates on a preclinical, clinical or commercial scale. The facilities used by our contract manufacturers to manufacture our product candidates are subject to various regulatory requirements and may be subject to the inspection of the FDA or other regulatory authorities. We do not control the manufacturing processes of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory

requirements, known as cGMPs. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable regulatory authorities in foreign jurisdictions, we may not be able to rely on their manufacturing facilities for the manufacture of our product candidates. In addition, we have limited control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds these facilities inadequate for the manufacture of our product candidates or if such facilities are subject to enforcement action in the future or are otherwise inadequate, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates.

We currently intend to supply our product candidates in all territories for our clinical development programs, and rely on third parties at key stages in our supply chain. For instance, the supply chains for our product candidates involve several manufacturers that specialize in specific operations of the manufacturing process, specifically, raw materials manufacturing, drug substance manufacturing and drug product manufacturing. As a result, the supply chain for the manufacturing of our product candidates is complicated, and we expect the logistical challenges associated with our supply chain to grow more complex as our product candidates are further developed.

We do not have any control over the process or timing of the acquisition or manufacture of materials by our manufacturers. We generally do not begin preclinical or clinical trials unless we believe we have access to a sufficient supply of a product candidate to complete such study. In addition, any significant delay in, or quality control problems with respect to, the supply of a product candidate, or the raw material components thereof, for an ongoing study could considerably delay completion of our preclinical or clinical trials, product testing and potential regulatory approval of our product candidates.

We have not yet engaged any manufacturers for the commercial supply of our product candidates. Although we intend to enter into such agreements prior to commercial launch of any of our product candidates, we may be unable to enter into any such agreement or do so on commercially reasonable terms, which could have a material adverse impact upon our business. Moreover, if there is a disruption to one or more of our third-party manufacturers' or suppliers' relevant operations, or if we are unable to enter into arrangements for the commercial supply of our product candidates, we will have no other means of producing our product candidates until they restore the affected facilities or we or they procure alternative manufacturing facilities or sources of supply. Our ability to progress our preclinical and clinical programs could be materially and adversely impacted if any of the third-party suppliers upon which we rely were to experience a significant business challenge, disruption or failure due to issues such as financial difficulties or bankruptcy, issues relating to other customers such as regulatory or quality compliance issues, or other financial, legal, regulatory or reputational issues. Additionally, any damage to or destruction of our third-party manufacturers' or suppliers' facilities or equipment may significantly impair our ability to manufacture our product candidates on a timely basis.

In addition, to manufacture our product candidates in the quantities we believe would be required to meet anticipated market demand, our third-party manufacturers would likely need to increase manufacturing capacity and we may need to secure alternative sources of commercial supply, which could involve significant challenges and may require additional regulatory approvals. In addition, the development of commercial-scale manufacturing capabilities may require us and our third-party manufacturers to invest substantial additional funds and hire and retain the technical personnel who have the necessary manufacturing experience. Neither we nor our third-party manufacturers may successfully complete any required increase to existing manufacturing capacity in a timely manner, or at all. If our manufacturers or we are unable to purchase the raw materials necessary for the manufacture of our product candidates on acceptable terms, at sufficient quality levels or in adequate quantities, if at all, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of such product candidates, if approved.

We rely on third parties in the conduct of all of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or meet expected deadlines, we may be unable to obtain regulatory approval for our product candidates.

We currently do not have the ability to independently conduct preclinical studies or clinical trials that comply with the regulatory requirements known as good laboratory practice, or GLP, requirements or GCP requirements,

respectively. The FDA and regulatory authorities in other jurisdictions require us to comply with GCP requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GLP-compliant preclinical studies and GCP-compliant clinical trials on our product candidates properly and on time. While we have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP-compliant preclinical studies and our GCP-compliant clinical trials play a significant role in the conduct of these studies and the subsequent collection and analysis of data. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our GLP-compliant preclinical studies and GCP-compliant clinical trials, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If the third parties conducting our preclinical studies or our clinical trials do not adequately perform their contractual duties or obligations, experience significant business challenges, disruptions or failures, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols or to GLPs or GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated. As a result we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, our business, financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If we are not successful in identifying, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our effort will focus on the continued development and potential approval of our current product candidates, a key element of our strategy is to identify, develop and commercialize a portfolio of products that address classical complement-mediated autoimmune and neurodegenerative diseases. A component of our strategy is to evaluate our product candidates in multiple indications based, in part, on our evaluation of certain biomarkers in a disease area. For example, we intend to evaluate ANX005 in neurodegenerative diseases, including amyotrophic lateral sclerosis, or ALS, and Huntington's disease, or HD; however, we are continuing to evaluate ANX005 in these patient populations, and even if we believe we have obtained positive clinical results in patients with one of these neurodegenerative diseases, such results may not be replicated in later studies evaluating ANX005 in patients with the same disease or across other neurodegenerative or autoimmune diseases. Even though we are currently developing a pipeline of product candidates, our development efforts may still fail to yield product candidates potentially suitable for commercialization for many reasons, including the following:

- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by physicians and patients.

We therefore cannot provide any assurance that we will be able to successfully identify or acquire additional product candidates, advance any of these additional product candidates through the development process, successfully commercialize any such additional product candidates, if approved, or assemble sufficient resources to identify,

acquire, develop or, if approved, commercialize additional product candidates. If we are unable to successfully identify, acquire, develop and commercialize additional product candidates, our commercial opportunities may be limited.

We face significant competition in an environment of rapid technological and scientific change, and our product candidates, if approved, will face significant competition, which may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do, and we may not be able to successfully compete.

The pharmaceutical, biopharmaceutical and biotechnology industries in particular are characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. Numerous companies are engaged in the development, patenting, manufacturing and marketing of healthcare products competitive with those that we are developing. We face competition from a number of sources, such as pharmaceutical, biopharmaceutical and biotechnology companies, generic drug companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, sales forces, manufacturing capabilities, research and development capabilities, clinical trial expertise, intellectual property portfolios, experience in obtaining patents and regulatory approvals for product candidates and other resources than we do. Some of the companies also have a broad range of other product offerings, large direct sales forces and long-term customer relationships with our target physicians, which could inhibit our market penetration efforts. Mergers and acquisitions in the pharmaceutical, biopharmaceutical and biotechnology industries 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.

Certain alternative treatments offered by competitors may be available at lower prices and may offer greater efficacy or better safety profiles. Furthermore, currently approved products could be discovered to have application for the intended indication of our product candidates, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA, or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. For example, with respect to ANX007, there are two approved products for GA which may pose competition for ANX007, if approved. For additional information regarding our competition, see the section titled "Business—Competition" in this Annual Report on Form 10-K.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Even if we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates or

any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical, biopharmaceutical and biotechnology products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the cost of the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amounts we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our investment in the development of product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. 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 applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other foreign jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amounts that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

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

We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell our product candidates, if approved, effectively in the United States and foreign jurisdictions or generate product revenue.

We currently do not have a marketing or sales organization. In order to commercialize our product candidates in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If any of our product candidates receive regulatory approval, we expect to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize each such product candidate, which will be expensive and time consuming. We have no prior experience in the marketing, sale and distribution of pharmaceutical, biopharmaceutical and biotechnology products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates. If we are not successful in commercializing our product candidates or any future product candidates, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of December 31, 2024, we had 100 full-time employees. We will need to continue to expand our managerial, operational, finance and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize our product candidates or any future product candidates. Our management and personnel, systems and facilities currently in place may not be adequate to support this or any future growth. Our need to effectively execute our growth strategy requires that we:

- manage our clinical trials effectively;
- successfully commercialize ANX005 and any of our other product candidates, if approved;
- identify, recruit, retain, incentivize and integrate additional employees, including sales personnel;
- manage our internal development and operational efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, financial and management controls, reports systems and procedures.

If management is unable to effectively manage our growth, our expenses may increase more than expected. Our future financial performance and our ability to compete effectively will depend, in part, on our ability to effectively manage any future growth.

If we fail to attract and retain senior management and key scientific personnel, our business may be materially and adversely affected.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and clinical and scientific personnel. We are highly dependent upon members of our senior management, as well as our senior scientists. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation or completion of our planned clinical trials or the commercialization of our product candidates or any future product candidates.

We cannot guarantee that we will not face turnover in the future. Our ability to execute our business strategies may be adversely affected by the uncertainty associated with any transition and the time and management attention needed to fill any vacant role could disrupt our business.

Competition for qualified personnel in the pharmaceutical, biopharmaceutical and biotechnology field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

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

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. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product 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 and breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our current or future product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize our current or any future product candidates.

If we are unable to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims, the commercialization of our current or any future product candidates we develop could be inhibited or prevented. We currently carry product liability insurance covering our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any 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 funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any of our product candidates, we intend to expand our insurance coverage to include the sale of such product candidate; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

While we have not entered into any collaboration agreements to date, we may seek collaboration arrangements for the commercialization, or potentially for the development, of certain of our product candidates depending on the merits of retaining commercialization rights for ourselves as compared to entering into collaboration arrangements. For example, certain of the disease areas that we believe our product candidates address, including, among others,

ophthalmic indications, require large, costly and later-stage clinical trials, which a collaboration partner may be better positioned to finance and/or conduct. In addition, a component of our strategy is to maximize the commercial value of our current and future product candidates, which may also strategically align with partnering commercial rights with partners that have larger and established sales organizations. To the extent that we decide to enter into collaboration agreements, we may face significant competition for appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain and challenging to manage. We may not be successful in our efforts to enter into collaboration agreements. The terms of collaborations or other arrangements that we may establish may not be favorable to us.

The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive products or their internal development of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- collaborators with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and collaborators that cause the delay or termination of the research, development or commercialization of our current or future product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, this may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- collaborators may own or co-own intellectual property covering products that result from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;
- disputes may arise with respect to the ownership of any intellectual property developed pursuant to our collaborations; and
- collaborators' sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Unfavorable global and macroeconomic or political conditions could adversely affect our business, financial condition or results of operations.

Our business is susceptible to general conditions in the global economy and in the global financial markets. Global financial crises and global or regional political disruptions have caused, and could in the future cause, extreme volatility in the capital and credit markets. A severe or prolonged economic downturn, including a recession or

depression, recent and potential bank failures, the current inflationary economic environment, rising interest rates, debt and equity market fluctuations, diminished liquidity and credit availability, increased unemployment rates, decreased investor and consumer confidence, supply chain challenges, natural catastrophes, the effects of climate change, regional and global conflicts and terrorist attacks or political disruption or turmoil could result in a variety of risks to our business, including weakened demand for our product candidates or any future product candidates, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our potential products. Any of the foregoing could materially and adversely affect our business, financial condition, results of operations and prospects, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend on may be adversely affected by earthquakes or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which has experienced both severe earthquakes and the effects of wildfires. We do not carry earthquake insurance. Earthquakes, wildfires or other natural disasters could severely disrupt our operations, and could materially and adversely affect our business, financial condition, results of operations and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are similarly vulnerable to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; U.S. federal and state healthcare fraud and abuse, data privacy laws and other similar non-U.S. laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare

programs, other sanctions, imprisonment, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our business involves the use of hazardous materials, and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates and other hazardous compounds. We and any third-party manufacturers and suppliers are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, and environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products.

We cannot guarantee that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, nor can we eliminate the risk of accidental contamination or injury from these materials. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

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

Risks Related to Intellectual Property

Our current and any future product candidates or products could be alleged to infringe patent rights and other proprietary rights of third parties, which may require costly litigation and, if we are not successful, could cause us to pay substantial damages and/or limit our ability to commercialize our products.

Our commercial success depends on our ability to develop, manufacture and market our current and any future product candidates that may be approved for sale, and to use our proprietary technology without infringing the patents and other proprietary rights of third parties. Intellectual property disputes can be costly to defend and may cause our business, results of operations and financial condition to suffer. We operate in an industry with extensive intellectual property litigation. As the pharmaceutical, biopharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that there may be patents issued to third parties that relate to our products and technology of which we are not aware or that we may need to challenge to continue our operations as currently contemplated.

Whether merited or not, we may face allegations that we have infringed the trademarks, copyrights, patents and other intellectual property rights of third parties, including patents held by our competitors or by non-practicing entities. We may also face allegations that our employees have misappropriated the intellectual property rights of their former employers or other third parties. Litigation may make it necessary to defend ourselves by determining the scope, enforceability and validity of third-party proprietary rights, or to establish our proprietary rights. Regardless of whether claims that we are infringing patents or other intellectual property rights have merit, such litigation can be time consuming, divert management attention and financial resources and are costly to evaluate and defend. There can be no assurance with respect to the outcome of any current or future litigation brought by or against us, and the outcome of any such litigation could have a material adverse impact on our business, results of operations and financial condition. Litigation is inherently unpredictable, and outcomes are uncertain. Further, as the costs and outcome of such litigation can vary significantly, it is difficult to estimate potential losses that may occur. As a result of such litigation, we may be required to stop treating certain conditions, obtain licenses or modify our products and features while we develop non-infringing substitutes, or may result in significant settlement costs or royalty obligations. For example, litigation can involve substantial damages for infringement, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees. We may also be prohibited from selling or licensing our products unless the third-party licenses rights to us, which it is not required to do at a commercially reasonable price or at all. If a license is available from a third party, we may have to pay substantial royalties or upfront fees or grant cross-licenses to intellectual property rights for our products. We may also have to redesign our products so they do not infringe third-party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time, during which our products may not be available for manufacture, use or sale. Accordingly, we are unable at this time to estimate the effects of these potential future lawsuits on our financial condition, operations or cash flows.

Additionally, some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. 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 material adverse effect on the price of our common stock. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Although we have reviewed certain third-party patents and patent filings that we believe may be relevant to our product candidates, we have not conducted a comprehensive freedom-to-operate search or analysis for any of our product candidates, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our product candidates. Additionally, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to commercialize our product candidates. Thus, we cannot guarantee that our activities related to their product candidates, or our commercialization, do not and will not infringe any third party's intellectual property.

In addition, patent applications in the United States and many other jurisdictions are typically not published until 18 months after the filing of certain priority documents (or, in some cases, are not published until they issue as patents), and publications in the scientific literature often lag behind actual discoveries. Therefore, we cannot be certain that others have not filed patent applications or made public disclosures relating to our technology or our contemplated technology. A third party may have already filed, and may in the future file, patent applications covering our product candidates or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, depending on whether the timing of the filing date falls under certain patent laws, we may have to participate in a priority contest (such as an interference proceeding) declared by the United States Patent and Trademark Office, or the USPTO, to determine priority of invention in the United States. The costs of patent litigation and other proceedings related to the protection of our global patent position could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our patent position with respect to such invention.

If we are unable to obtain, maintain and enforce intellectual property protection directed to our current and any future technologies that we develop, others may be able to make, use or sell products substantially the same as ours, which could adversely affect our ability to compete in the market.

The market for pharmaceuticals and biopharmaceuticals is highly competitive and subject to rapid technological change. Our success depends, in part, upon our ability to maintain a competitive position in the development and protection of technologies and any future products for use in these fields and upon our ability to obtain, maintain and enforce our intellectual property rights. We seek to obtain and maintain patents and other intellectual property rights to restrict the ability of others to market products that misappropriate our technology and/or infringe our intellectual property to unfairly and illegally compete with any future products. If we are unable to protect our intellectual property and proprietary rights, our competitive position and our business could be harmed, as third parties may be able to make, use or sell products that are substantially the same as any future products we may sell without incurring the sizeable development and licensing costs that we have incurred, which would adversely affect our ability to compete in the market.

We use a combination of patents, trademarks, know-how, confidentiality procedures and contractual provisions to protect our proprietary technology. However, these protections may not be adequate and may not provide us with any competitive advantage. For example, patents may not issue from any of our currently pending or any future patent applications, and our issued patents and any future patents that may issue may not survive legal challenges to their scope, validity or enforceability, or provide significant protection for us.

We have not pursued or maintained, and may not pursue or maintain in the future, patent protection for our product candidates in every country or territory in which we may sell our products. In addition, we cannot be sure that any of our pending patent applications or pending trademark applications will issue or that, if issued, they will issue in a form that will provide adequate protection for our products. The USPTO, patent offices in other jurisdictions, or judicial or other bodies in any jurisdiction may deny or significantly narrow claims made under our patent applications, and claims in our issued patents may be invalidated, may be designed around or may otherwise be unable to provide us with protection for our products. Further, the USPTO, trademark offices in other jurisdictions, or judicial or other bodies in any jurisdiction may deny our trademark applications and, even if published or registered, these trademarks may not effectively protect our brand and goodwill. Like patents, trademarks also may be successfully opposed or challenged.

We cannot be certain that the steps we have taken will prevent unauthorized use or unauthorized reverse engineering of our technology that is material to our business. Moreover, third parties may independently develop technologies that are competitive with ours and such competitive technologies may or may not infringe our intellectual property. The enforcement of our intellectual property rights also depends on the success of any legal actions we may take against these third parties in the respective country or forum, but these actions may not be successful. As with all granted intellectual property, such intellectual property may be challenged, invalidated or circumvented, may not provide protection and/or may not prove to be enforceable in actions against specific alleged infringers.

If we or any future collaborators we may have were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates or future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. 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 obviousness or lack of novelty, enablement or 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. Third parties may also raise similar claims before the USPTO even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, or that a defendant would not prevail on an assertion of invalidity based on prior art that we were aware of during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if claims in our patents survive assertions of invalidity and unenforceability, they may not be broad enough to prevent others from marketing products similar to ours or designing around our patents. For example, third parties may be able to make products that are similar to ours but that are not covered by the claims of our patents. The claims of our issued patents or patent applications when issued may not cover our product candidates or any future products that we develop.

Patent law can be highly uncertain and involve complex legal and factual questions for which important principles remain unresolved. In the United States and in many other jurisdictions, policies regarding the breadth of claims allowed in patents can be inconsistent. The U.S. Supreme Court and the Court of Appeals for the Federal Circuit have made, and will likely continue to make, changes in how the patent laws of the United States are interpreted. Similarly, courts in other jurisdictions have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by U.S. and international legislative bodies. Those changes may materially affect the patents and patent applications of our licensors, our existing or future patents and patent applications and our ability to obtain additional patents in the future.

Patent reform legislation in the United States could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or Leahy-Smith Act, was signed into law. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation and switch the U.S. patent system from a "first-to-invent" system to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, which could have a material adverse effect on our business and financial condition. Any future changes in the patent laws of the United States, or even the possibility of such changes, may further increase these uncertainties and costs.

The USPTO and various patent agencies in other jurisdictions require compliance with a number of procedural, documentary, fee, annuity payment and other provisions to maintain patent applications and issued patents. Although 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 with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

In addition, we have a number of patents and patent applications outside of the United States and expect to continue to pursue patent protection in many of the significant markets in which we intend to do business. The laws of some international jurisdictions do not protect intellectual property rights to the same extent as laws in the United States, and many companies have encountered significant difficulties in obtaining, protecting and defending such rights in certain jurisdictions outside of the United States. If we encounter such difficulties or we are otherwise precluded from effectively protecting our intellectual property rights in international jurisdictions, our business, financial condition, results of operations and prospects could be materially and adversely affected. Earlier patent filings in certain international countries may also permit third parties to allege priority to certain technology in those countries.

Patent terms may be shortened or lengthened in certain jurisdictions by, for example, terminal disclaimers, patent term adjustments, supplemental protection certificates and patent term extensions. Patent term extensions and supplemental protection certificates, and the like, may be impacted by the regulatory process and may not significantly lengthen patent term. Non-payment or delay in payment of patent extension filing (including any patent term extension or adjustment filing) fees, whether intentional or unintentional, may also result in the loss of patent rights important to our business. Certain countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to other parties. In addition, many countries limit the enforceability of patents against other parties, including government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of any patents.

Monitoring unauthorized use of our intellectual property is difficult and costly. From time to time, we review our competitors' products, and may in the future seek to enforce our patents or other rights against potential infringement. However, the steps we have taken to protect our proprietary rights may not be adequate to prevent misappropriation of our intellectual property. We may not be able to detect unauthorized use of, or take appropriate steps to enforce, our intellectual property rights. Our competitors may also independently develop similar technology. Any inability to meaningfully protect our intellectual property could result in competitors offering products competitive to our products. In addition, we may need to defend our patents from third-party challenges, such as interferences, derivation proceedings, re-examination proceedings, post-grant review, inter partes review, third-party submissions, oppositions, nullity actions or other patent proceedings. We may need to initiate infringement claims or litigation.

Adverse proceedings such as litigation can be expensive, time consuming and may divert the efforts of our technical and managerial personnel, which could in turn materially and adversely affect our business, financial condition, results of operations and prospects, whether or not we receive a determination favorable to us. In addition, in an infringement proceeding, a court or other judicial body may decide that the patent we seek to enforce is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that the patent in question does not cover the technology in question or that stopping the other party would harm the public interest. An adverse result in any litigation could put one or more of our patents at risk of being invalidated or interpreted narrowly. Some of our competitors may be able to devote significantly more resources to intellectual property litigation, and may have significantly broader patent portfolios to assert against us if we assert our rights against them. Further, because of the substantial discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be disclosed or otherwise compromised during litigation.

We may not be able to correctly estimate or control our future operating expenses in relation to obtaining intellectual property, enforcing intellectual property and/or defending intellectual property, which could affect operating expenses. Our operating expenses may fluctuate significantly in the future as a result of a variety of factors, including the costs of preparing, filing, prosecuting, defending and enforcing patent and trademark claims and other intellectual property-related costs, including adverse proceedings and litigation costs.

If we are unable to prevent disclosure of our trade secrets or other confidential information to third parties, our competitive position may be impaired.

In addition to the protection afforded by patents, we rely on confidentiality agreements to protect confidential information and proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. Agreements or security measures may be breached and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position. Furthermore, the laws of some other jurisdictions do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and in other jurisdictions. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. The failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

We are or may become a party to licenses that give us rights to third-party intellectual property that are necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements, we are or may become obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. These fees may be significant, which could make it difficult for us to achieve or maintain profitability. In addition, under certain of such agreements, we are or may become required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business, harming our ability to develop, manufacture and/or commercialize our platform or product candidates. If the licensor retains control of prosecution of the patents and patent applications licensed to us, we may have limited or no control over the manner in which the licensor chooses to prosecute or maintain its patents and patent applications and have limited or no right to continue to prosecute any patents or patent applications that the licensor elects to abandon.

If the licensor retains control of prosecution of the patents and patent applications licensed to us, we may have limited or no control over the manner in which the licensor chooses to prosecute or maintain its patents and patent applications and have limited or no right to continue to prosecute any patents or patent applications that the licensor elects to abandon.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

Our intellectual property agreements with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

Certain provisions in our intellectual property agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could affect the scope of our rights to the relevant intellectual property or technology, or affect financial or other obligations under the relevant agreement, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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. Our assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

We may wish to form collaborations in the future with respect to our product candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.

Our product candidates may also require specific components to work effectively and efficiently, and rights to those components may be held by others. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies, which could harm our business prospects, financial condition and results of operations.

We jointly own certain patent rights with third parties. Our ability to out-license these patent rights, or to prevent the third party from out-licensing these patent rights, may be limited in certain countries.

We jointly own certain patents and patent applications with third parties, and may jointly own patents and patent applications with third parties in the future. Unless we enter into an agreement with the joint owner, we will be subject to certain default rules pertaining to joint ownership. Certain countries require the consent of all joint owners to license jointly owned patents, and if we are unable to obtain such consent from the joint owner, we may not be able to license our rights under these patents and patent applications. In certain other countries, including the United States, the joint owner could license its rights under these patents and patent applications to another party without our consent and without any duty of accounting to us.

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

We may also be subject to claims that former employees, any future collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights and could even face litigation for infringing patents that we had regarded as ours. 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 distraction to management and other employees.

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

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 registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, declared generic or conflict with third-party rights. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition with potential partners, physicians or patients in our markets of interest. During trademark registration proceedings, our trademark applications may be rejected. Although we are 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 can oppose pending trademark applications and seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Furthermore, third parties may file first for our trademarks in certain countries. If they succeeded in registering such trademarks, and if we are not successful in challenging such third-party rights, we may not be able to use these trademarks to market our future products in those countries. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. In such cases, over the long term, if we are unable to establish and maintain name recognition based on our trademarks and trade names, then our commercial success abilities may be impacted.

Moreover, any name we propose to use with our product candidates in the United States or any other country must be approved by the FDA, EMA or any other relevant health authority regardless of whether we have registered it, or applied to register it, as a trademark. The FDA as well as EMA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA, EMA or any other relevant approval authority objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable

trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA, EMA or any other relevant approval authority.

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

Filing and prosecuting patent applications, and defending patents, related to our product candidates in all countries throughout the world would be prohibitively expensive, and 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 may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with any future products we may sell, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals and biopharmaceuticals, 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 generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. 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.

Risks Related to Government Regulation

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMPs and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

We will have to comply with requirements concerning advertising and promotion for any future products. Promotional communications with respect to prescription drugs and biologics are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. We may not promote products for indications or uses for which they do not have approval. The holder of an approved application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety, purity, potency and/or efficacy of our products in general or in specific patient subsets. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with

the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from any future products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our results of operations will be adversely affected.

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

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, 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 enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. The ACA, among other things: (i) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (ii) 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 some government healthcare programs; (iii) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (iv) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (v) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (vi) 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; and (vii) established a Center for Medicare and Medicaid Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been amendments and judicial, Congressional and executive branch challenges to certain aspects of the ACA. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was

signed into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how other healthcare reform measures will impact our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's AMP, effective January 1, 2024. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models.

In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. Most recently, the IRA, among other things, (1) directs the U.S. Department of Health and Human Services, or HHS to negotiate the price of certain single-source drugs and biologics that have been on the market for at least 7 years covered under Medicare, or the Medicare Drug Price Negotiation Program, and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions began to take effect beginning fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon reimbursement price of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, particularly in light of the recent change in administration, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could materially and adversely affect our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or judicial action in the United States, the EU or any other jurisdiction. 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 product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

If we develop a small molecule product candidate that obtains regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, a pharmaceutical manufacturer may submit an abbreviated new drug application, or ANDA, seeking approval of a generic version of an approved, small molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act that references the FDA's prior findings of safety and effectiveness of the small molecule innovator product. For example, a 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and review) of an ANDA or 505(b)(2) NDA. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the Orange Book. If there are patents listed in the Orange Book for a product, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in their applications what is known as a "Paragraph IV" certification, challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the patent owner and NDA holder and if, within 45 days of receiving notice, either the patent owner or NDA holder sues for patent infringement, approval of the ANDA or 505(b)(2) NDA is stayed for up to 30 months.

Accordingly, if our small molecule program results in a product that is approved, competitors could submit ANDAs for generic versions of our small molecule drug products or 505(b)(2) NDAs that reference our small molecule drug products. If there are patents listed for our small molecule drug products in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include, without limitation:

- the U.S. federal civil and criminal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or

entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal false claims laws, including the False Claims Act, which can be enforced through whistleblower actions, and civil monetary penalties laws, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the Health Insurance Portability and Accountability Act of 1996, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians, as defined by such law, certain non-physician providers such as physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state and local laws that require the registration of pharmaceutical sales representatives; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and
- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office and foreign political parties or officials thereof.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, such as the provision of stock options to physicians who may influence the ordering, prescribing or use of our product candidates, if approved, as compensation for consulting services, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, disgorgement, imprisonment,

contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming and may require significant personnel resources. Even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Risks Related to Our Common Stock

Our stock price has been volatile, and could in the future be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

The stock price of our common stock has been, and could in the future be, subject to substantial volatility and wide fluctuations in response to various factors, some of which are beyond our control. In particular, the stock prices for pharmaceutical, biopharmaceutical and biotechnology companies have been highly volatile as a result of extreme volatility and disruptions in the global economy, including rising inflation and interest rates, declines in economic growth, the war between Russia and Ukraine and uncertainty about economic stability, including a potential recession. These factors include those discussed in this "Risk Factors" section and others such as:

- results from, and delays in, our clinical trials for our product candidates or any other future clinical development programs;
- announcements of regulatory approval or disapproval of our current or any future product candidates;
- failure or discontinuation of any of our research and development programs;
- the termination of any of our existing license agreements;
- announcements relating to any future licensing, collaboration or development agreements;
- delays in the commercialization of our current or any future product candidates;
- public misperception regarding the use of our product candidates;
- acquisitions and sales of new products or product candidates, technologies or businesses;
- manufacturing and supply issues related to our product candidates for clinical trials or future product candidates for commercialization;
- quarterly variations in our results of operations or those of our competitors;
- changes in earnings estimates or recommendations by securities analysts;
- announcements by us or our competitors of new products or product candidates, significant contracts, commercial relationships, acquisitions or capital commitments;
- developments with respect to intellectual property rights;
- our commencement of, or involvement in, litigation;
- changes in financial estimates or guidance;
- any major changes in our board of directors or management;
- new legislation or regulation in the United States relating to the sale or pricing of pharmaceuticals;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- product liability claims or other litigation or public concern about the safety of our product candidates;
- market conditions in the pharmaceutical, biopharmaceutical and biotechnology sectors;
- general economic conditions in the United States and abroad, the current inflationary economic environment, rising interest rates and global health concerns;
- sales of our common stock, including sales by our officers, directors and specific existing stockholders; and

- the issuance of shares of our common stock pursuant to the exercise of outstanding warrants.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the stock price or liquidity of our common stock.

We are a "smaller reporting company," and as a result of the reduced disclosure and governance requirements applicable to smaller reporting companies, our common stock may be less attractive to investors.

We are a smaller reporting company and are therefore entitled to take advantage of many of the same exemptions from disclosure requirements as an emerging growth company, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, as a smaller reporting company with less than $100 million in annual revenue, we are exempt from the requirement to obtain an auditor attestation on the effectiveness of our internal control over financial reporting provided in Section 404(b) of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects.

We incur significant costs as a result of operating as a public company, and our management needs to devote substantial time to compliance initiatives. We may fail to comply with the rules that apply to public companies, which could result in sanctions or other penalties that could materially and adversely affect our business, financial condition, results of operations and prospects.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of the Nasdaq Stock Market and the rules of the SEC require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel needs to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, these reporting requirements, rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

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

We are subject to Section 404 of the Sarbanes-Oxley Act, or Section 404, and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Pursuant to Section 404(a), we are required to file with the SEC an annual management assessment of the effectiveness of our internal control over financial reporting. Because we re-qualified as a smaller reporting company and we have less than $100 million in annual revenue, as of December 31, 2024, we are a non-accelerated filer and are not required to comply with the auditor attestation requirements regarding the effectiveness of our internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act until we become an accelerated filer or large accelerated filer.

Our management's assessment needs to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual and interim financial statements will not be detected or prevented on a timely basis. If we identify one or more material weaknesses in our internal control over financial reporting, we will be unable

to assert that our internal controls are effective. The effectiveness of our controls and procedures may be limited by a variety of factors, including:

- faulty human judgment and simple errors, omissions or mistakes;
- fraudulent action of an individual or collusion of two or more people;
- inappropriate management override of procedures; and
- the possibility that any enhancements to controls and procedures may still not be adequate to assure timely and accurate financial control.

While we believe our internal control over financial reporting is currently effective, the effectiveness of our internal controls in future periods is subject to the risk that our controls may become inadequate because of changes in conditions. Establishing, testing and maintaining an effective system of internal control over financial reporting requires significant resources and time commitments on the part of our management and our finance staff, may require additional staffing and infrastructure investments and would increase our costs of doing business. We can give no assurance that material weaknesses in our internal control over financial reporting will not be identified in the future. Our failure to implement and maintain effective internal control over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements and cause us to fail to meet our reporting obligations. Effective internal control over financial reporting is necessary for us to provide reliable and timely financial reports and, together with adequate disclosure controls and procedures, are designed to reasonably detect and prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would materially and adversely affect our business, financial condition, results of operations and prospects.

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

As of December 31, 2024, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned a majority of our outstanding voting stock. In addition, in our 2023 and 2024 financings, certain of the holders of 5% or more of our capital stock acquired pre-funded warrants to purchase shares of our common stock (which are immediately exercisable and have an exercise price of $0.001 per share) or common warrants to purchase shares of our common stock. Until exercised, the shares issuable upon the exercise of the pre-funded warrants and the common warrants are not included in the number of our outstanding shares of common stock. If such holders exercise their warrants, then the shares of our capital stock beneficially owned by our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates would increase significantly. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

Our current shares outstanding and resulting market valuation do not reflect shares of our common stock issuable upon the exercise of pre-funded warrants and common warrants that are exercisable at the discretion of the holders of such warrants. If we sell shares of our common stock in the future, stockholders may experience immediate dilution. Stockholders may be unable to compute the dilutive impact of future financings.

We may from time to time issue additional shares of common stock, and as a result, our stockholders would experience immediate dilution. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. For example, in March 2024, we entered into a sales agreement with Cowen and Company LLC, or TD Cowen, as sales agent,

pursuant to which we may issue and sell shares of our common stock for an aggregate maximum offering price of $100.0 million under an at-the-market offering program under which we have sold approximately $4.5 million of shares of our common stock as of the date of this Annual Report on Form 10-K. In addition, in July 2022, December 2023, and June 2024, we closed financings which included the sale of pre-funded warrants or common warrants to purchase shares of our common stock. Until exercised, the shares issuable upon the exercise of the pre-funded warrants or the common warrants are not included in the number of our outstanding shares of common stock. If we issue common stock or securities convertible into common stock in the future, our stockholders would experience additional dilution and such dilutive impact may be difficult to compute.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the stock price of our common stock could decline. As of December 31, 2024, the number of shares of our common stock outstanding was 109,381,556. This number does not include 38,543,577 shares of common stock issuable upon the exercise of pre-funded warrants or 8,104,615 shares of common stock issuable upon the exercise of common warrants. On August 12, 2024, we filed a resale registration statement on Form S-3, pursuant to which, entities and trusts affiliated with Muneer Satter, a member of our board of directors, can sell up to 3,000,000 shares of common stock. Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, may reduce the stock price of our common stock.

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

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a rolling three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre-change NOLs or credits if we undergo a future ownership change.

We completed a study through December 31, 2024, to determine whether an ownership change had occurred under Section 382 or 383 of the Code, and we determined that ownership changes occurred in 2011, 2014, 2020 and 2023. We have identified $0.1 million and $34.7 million of federal and state NOLs, respectively, that will expire unused due to ownership changes, and federal credits of $4.3 million that will not be able to be utilized due to ownership change limitation and excluded these amounts from deferred tax asset balances as of December 31, 2024. Federal NOLs of $367.6 million and state and local NOLs of $189.2 million are not expected to expire unutilized as a result of ownership changes identified through December 31, 2024.

Our ability to use NOLs, research and development credit carryforwards and other tax attributes to reduce future taxable income and tax liabilities may be further limited as a result of shifts in our stock ownership subsequent to December 31, 2024. As a result, even if we attain profitability, our ability to use our pre-change NOLs or other pre-change tax attributes to offset United States federal and state taxable income may be subject to further limitations.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;

- the exclusive right of our board of directors to elect a director to fill a vacancy, however occurring, including by an expansion of the board of directors, which prevents stockholders from being able to fill vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including voting or other rights or preferences, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

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 amended and restated certificate of incorporation and amended and restated 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 amended and restated 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 amended and restated 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 amended and restated 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; and
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

While we maintain a directors' and officers' insurance policy, such insurance may not be adequate to cover all liabilities that we may incur, which may reduce our available funds to satisfy third-party claims and may adversely impact our cash position.

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

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

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

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

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

General Risk Factors

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and 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 may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with any future products we may sell, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals and biopharmaceuticals, 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 generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. 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.

Changes in tax laws and regulations may have a material adverse effect on our business, financial condition and results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of any of our future domestic and foreign earnings. Any new taxes could adversely affect our domestic and international business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. Generally, future changes in applicable U.S. and non-U.S. tax laws and regulations, or their interpretation and application, could have an adverse effect on our business, financial conditions and results of operations. We are unable to predict whether such changes will occur and, if so, the ultimate impact on our business.

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

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or

import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Cybersecurity risks and the failure to maintain the security, confidentiality, integrity, or availability of our information technology systems or data, and those maintained on our behalf, could lead to adverse consequences that materially adversely affect our business, including, without limitation, regulatory investigations or actions, a material interruption to our operations, including clinical trials, damage to our reputation and/or subject us to costs, loss of customers or sales, fines and penalties or lawsuits.

We collect and maintain information in digital and other forms that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we and the third parties with whom we work process sensitive data. We have established physical, electronic and organizational measures designed to safeguard and secure our systems in an effort to prevent a data compromise; there can, however, be no assurance that these measures will be or have been effective. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors have access to our sensitive data. Our information technology systems and infrastructure, and those of any future collaborators and our contractors, consultants, vendors and other third parties with whom we work, are vulnerable to and have experienced attacks, damage and interruption from cyber-attacks, malicious internet-based activity, online and offline fraud, computer viruses, malware (e.g., ransomware), credential stuffing, credential harvesting, supply-chain attacks, natural disasters, fire, terrorism, war, telecommunication and electrical failures, attacks enhanced or facilitated by AI, denial or degradation of service attacks, hacking, sophisticated nation-state and nation-state supported actors, phishing and other social engineering attacks (including through deep fakes, which are increasingly more difficult to identify), attachments to emails, fraud, personnel misconduct or error, server malfunctions, software or hardware failures, loss or theft of data or information technology assets, unauthorized access or use, and other similar threats. In particular, ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, loss of sensitive data, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments.

The risk of a security breach or disruption, particularly through cyber-attacks, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. The prevalent use of mobile devices that access sensitive data also increases the risk of lost or stolen devices, security incidents and data security breaches, which could lead to the loss or other compromise of sensitive data. In a hybrid working environment, we also face risks of a security breach or disruption due to our reliance on internet technology and the number of our personnel who are working remotely, which creates additional opportunities for cyber criminals to exploit vulnerabilities or other weaknesses. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. We may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. Security breaches may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

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

We rely upon third-party service providers and technologies to operate critical business systems and process sensitive data in a variety of contexts, including, without limitation, third-party providers of cloud-based infrastructure, encryption and authentication technology, employee email, and other functions. Our ability to monitor these third parties' security practices is limited, and these third parties may not have adequate security measures in place. Our

third-party service providers have experienced and may experience in the future a security incident or other interruption. For example, one of our third-party drug component suppliers experienced a cyber-attack, which did not materially impact our operations. In addition, in 2024, one of our vendors experienced a cyber-attack which resulted in our access to the third-party system being unavailable to us for a brief period of time before being restored, which we concluded did not materially impact our operations or clinical data. These and similar incidents have and could lead to business interruptions and additional costs. Any significant system failure, accident or security breach and resulting interruptions in our operations or our critical third parties' operations could result in a material disruption of our product development programs, and ultimately, our financial results. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. The costs to us to prevent, investigate, mitigate and remediate security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures designed to protect our data security and information technology systems and sensitive data, our efforts to address these problems may not be successful, and these problems have and may in the future result in unexpected interruptions, delays, cessation of service, negative publicity and other harm to our business and our competitive position. Any security compromise affecting us or the third parties with whom we work, or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures and lead to regulatory scrutiny. Moreover, if a security breach affects our systems or results in the unauthorized access to or unauthorized use, disclosure, release or other processing of sensitive data, we may be required, or we may voluntarily choose, to notify individuals, governmental authorities, supervisory bodies, the media and other parties, or to take other actions, such as providing credit monitoring and identity theft protection services pursuant to privacy and security laws or other obligations, and our reputation could be materially damaged. We would also be exposed to a risk of loss, governmental investigations or enforcement, or litigation (including class action claims) and other potential liability, which could materially adversely affect our business, results of operations and financial condition. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

Actual or perceived failure to comply with applicable data protection laws, regulations, standards, contractual obligations and other requirements related to data privacy and security could lead to government enforcement actions and civil or criminal penalties, private litigation (including class actions) or adverse publicity and otherwise could negatively affect our results of operations and business.

In the ordinary course of business we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive and confidential information, including proprietary and confidential business data, trade secrets, intellectual property, data we may collect about trial participants in connection with clinical trials, sensitive third-party data, and employee data (collectively, sensitive data). Our data processing activities actually or may subject us to numerous privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. Data privacy and security obligations are stringent and changing, with new data privacy and security laws being proposed or enacted. Preparing for and complying with these obligations requires significant resources and has in the past necessitated and may in the future necessitate changes to our information technologies, systems, and practices and to those of any third parties with whom we work. The laws and regulations that affect our ability to operate include, but may not be limited to:

- the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, or HIPAA,

which imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. Depending on the facts and circumstances, however, we could be subject to significant administrative, civil and criminal penalties if we obtain, use or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA;

- the California Consumer Privacy Act of 2018, or CCPA, which requires covered businesses to provide certain disclosures in privacy notices to California residents, including consumers, business representatives, and employees, and requires businesses honor certain requests of California residents to exercise certain privacy rights. The CCPA provides for administrative fines, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws may impact our business activities depending on how it is interpreted. Further, the amendments to the CCPA expanded the CCPA's requirements, including by adding a right for individuals to correct their personal data and establishing a regulatory agency to implement and enforce the law. Additional compliance investment and business process changes may be required in an effort to address data protection laws. Similar laws have been passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that make compliance challenging; and
- foreign data protection laws, including the European Union's General Data Protection Regulation, or EU GDPR, and the United Kingdom GDPR, or UK GDPR, which contain provisions specifically directed at the processing of health data and, more broadly, impose significant and complex compliance burdens on processing personal data. Under the EU and UK GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines for noncompliance of up to €20 million under the EU GDPR (£17.5 million under the UK GDPR) or 4% of annual global revenue of the noncompliance company, whichever is greater. Noncompliance with the EU and UK GDPR could also result in private litigation related to the processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. These laws such as the EU and UK GDPR impose numerous requirements for the collection, use, storage and disclosure of personal data of data subjects, including requirements relating to providing notice to and obtaining consent from data subjects, personal data breach notification, cross-border transfers of personal data, and honoring and providing for the rights of individuals in relation to their personal data, including the right to access, correct and delete their data. Among other requirements, the EU and UK GDPR regulate transfers of personal data subject to the EU and UK GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EU and the United States remains uncertain.

In the ordinary course of business, we transfer personal data from Europe and other jurisdictions to the United States and other countries. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States or other relevant countries. If there were no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some

European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the EU GDPR's cross-border data transfer limitations. Other jurisdictions (including the US) have adopted or may adopt stringent data localization and cross-border data transfer laws. For example, regulators in the United States have enacted certain restrictions on cross-border personal data transfers.

In addition to data privacy and security laws, clinical trial subjects about whom we or any of our potential collaborators obtain information, as well as the providers who share this information with us, have and may in the future limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could materially and adversely affect our business, financial condition, results of operations and prospects. We also publish policies, marketing materials, and other statements regarding data privacy and security. Regulators are increasingly scrutinizing these statements, and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Our personnel use generative artificial intelligence, or AI, technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.

Although we work to comply with applicable privacy and data security laws, regulations and standards, contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Compliance with these data protection obligations has in the past and may in the future require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use, disclose and otherwise process personal data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Any actual or perceived failure to comply by us or our personnel, representatives, contractors, consultants, collaborators, or other third parties could result in government investigations and/or enforcement actions, fines, civil or criminal penalties, additional reporting requirements and/or oversight, bans on processing personal data (including clinical trial data), orders to destroy or not use personal data, private litigation (including class action claims) and mass arbitration demands, adverse publicity and could otherwise negatively affect our results of operations and business.

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

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and results of operations fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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

In the past, companies that have experienced volatility in the market price of their securities have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Regardless of the merits or the ultimate results of such litigation, securities litigation brought against us could result in substantial costs and divert our management's attention from other business concerns.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity

Risk management and strategy

We have implemented a risk-based approach designed to identify, assess and manage cybersecurity threats that could materially affect our business and information systems. We attempt to identify and assess risks from cybersecurity threats by evaluating our threat environment using various methods including, for example: maintaining manual and automated tools, subscribing to reports and services that identify cybersecurity threats, evaluating threats reported to us, and completing third-party cybersecurity threat assessments.

We use cybersecurity consultants and penetration testing firms in an effort to identify, assess, and manage material risks from cybersecurity threats. We use third-party service providers in various elements to our business operations such as data hosting providers. To help manage cybersecurity risks associated with our use of third-party service providers, we primarily engage with industry-preferred service providers, and we also contractually require service providers with access to personal, confidential, or proprietary information to maintain data security controls and practices.

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including "*Cybersecurity risks and the failure to maintain the security, confidentiality, integrity, or availability of our information technology systems or data, and those maintained on our behalf, could lead to adverse consequences that materially adversely affect our business, including, without limitation, regulatory investigations or actions, a material interruption to our operations, including clinical trials, damage to our reputation and/or subject us to costs, loss of customers or sales, fines and penalties or lawsuits.*"

Governance

Our board of directors addresses our cybersecurity risk management as part of its general oversight function. The audit committee is responsible for advising on our cybersecurity risk management processes, including oversight of mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and risk management processes are managed by certain members of our management, including our CFO (who has prior experience in strategic business operations). Our CFO has supervisory responsibility over IT and cybersecurity functions. Our management is responsible for helping to integrate cybersecurity risk considerations into our overall risk management strategy, helping prepare for and respond to cybersecurity incidents, and reviewing security assessments and other security-related reports. Our incident response team is responsible for remediating cybersecurity incidents of which they are notified.

We maintain a cybersecurity policy, reviewed with our audit committee, which is designed to address cybersecurity risks to us (including by escalating certain cybersecurity incidents to members of management and the board of the audit committee, in each case depending on the circumstances). We also maintain incident response procedures designed to assist us in responding to cybersecurity incidents.

Item 2. Properties.

Our corporate headquarters are located in Brisbane, California, where we lease approximately 65,818 square feet of office and laboratory space. The contractual term of the Brisbane lease commenced in November 2021 and will end in October 2031, with an option to extend for an additional ten years.

Item 3. Legal Proceedings.

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties, and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation, and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny

coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our business, results of operations and financial condition. Additionally, any such claims, whether or not successful, could damage our reputation and business.

Item 4. Mine Safety Disclosures.

None.

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 has been traded on the Nasdaq Global Select Market under the symbol "ANNX" since July 24, 2020. Prior to that, there was no public market for our common stock.

Stockholders

As of the date of this Annual Report on Form 10-K, there were 28 holders of record of our common stock. 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. This 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, and do not anticipate declaring or paying in the foreseeable future, any cash dividends on our capital stock. Any future determination as to the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to applicable laws and will depend on then existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects, and other factors our board of directors may deem relevant.

Securities Authorized for Issuance under Equity Compensation Plans

See the section titled "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" for information regarding securities authorized for issuance.

Recent Sales of Unregistered Securities

None.

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.

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K.

In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, beliefs, and expectations, and involve risks and uncertainties. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report on Form 10-K, particularly in the sections titled "Special Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

We are a clinical-stage biopharmaceutical company pioneering a new class of complement medicines for people living with devastating inflammatory-related diseases. The classical complement pathway is a core component to the body's immune system that activates a powerful inflammatory cascade. We believe that by stopping the classical complement pathway at its start by targeting C1q, the initiating molecule of the classical complement pathway, our approach may have the potential to provide more complete protection against complement-mediated disorders of the body, brain and eye.

Using our proprietary platform, we are identifying and characterizing the role of the classical complement pathway in three therapeutic areas—autoimmune, neurodegeneration and ophthalmology. In so doing, we are advancing a pipeline of product candidates designed to block the early classical cascade and all downstream pathway components and their tissue-damaging functions. Our goal is to suppress excessive or aberrant classical complement activity that contributes to chronic inflammation and tissue damage to slow or even halt disease progression, while preserving the beneficial immune functions of the lectin and alternative complement pathways involved in the clearance of pathogens and damaged cells. We have demonstrated robust target engagement in the body, brain and eye, and clinical proof of concept in multiple diseases, and have focused our resources on development of three priority programs:

- **Guillain-Barré Syndrome, or GBS:** We are advancing our lead candidate, ANX005, an investigational, full-length monoclonal antibody, or mAb, formulated for intravenous administration as the potential first targeted treatment for patients with GBS. GBS is a rare antibody-mediated autoimmune disease that is the most common cause of acute neuromuscular paralysis, with no therapies in the United States approved by the FDA. We believe maximum suppression of C1q and the classical complement cascade early in the disease process may act to rapidly prevent complement-mediated nerve damage and irreversible neurological disability. In a prior Phase 1b placebo-controlled proof-of-concept trial, a single dose of ANX005 showed rapid and consistent improvement in muscle strength that translated into observable gains in health status, including a reduction in the need of mechanical ventilation, as well as a reduction in nerve damage and clinical function. In 2024, we completed a Phase 3 trial in 241 patients, which showed ANX005 helped patients improve sooner with rapid increase in muscle strength and more complete functional recovery than placebo through six months, and provided an important benefit in the burden of care by enabling patients to walk or be off ventilation earlier. In addition, we completed a Real World Evidence, or RWE, study that matched ANX005-treated patients from the Phase 3 study with a western world patient population from the International Guillain-Barré Syndrome Outcomes Study, or IGOS, predominantly from Europe and North America treated with current standards of care (intravenous immunoglobulin, or IVIg, or plasma exchange, or PE). Consistent with the Phase 3 trial, ANX005 showed a rapid increase in muscle strength with more complete recovery over IVIg or PE. We anticipate the Phase 3 and RWE results to support a comprehensive dataset for our Biologics License Application, or BLA, and are targeting the first half of 2025 for our pre-BLA meeting with the FDA ahead of our planned BLA submission. ANX005 has been granted Fast Track and orphan drug designation for the treatment of GBS from the FDA. ANX005 has also been granted orphan designation from the European Medicines Agency, or EMA.
- **Geographic Atrophy, or GA:** We are advancing ANX007, an antigen-binding fragment, or Fab, formulated for intravitreal administration, as the first potential program with a global registration path to approval in Europe and the United States for the treatment of dry AMD with GA. Dry AMD with GA is

a leading cause of vision loss in the elderly, that affects more than an estimated eight million people globally, and there are no approved therapies targeting the preservation of vision in this disease. ANX007 is designed to block C1q locally in the eye, to provide more complete protection against excess classical complement activity and the loss of photoreceptor neurons. It is the only investigational therapy in GA to show significant vision preservation on assessments of best corrected visual acuity, or BCVA, and low luminance visual acuity, or LLVA, demonstrating significant protection from vision loss in both normal and low light conditions, as well as significant preservation of central retinal photoreceptors necessary for visual acuity as demonstrated in the Phase 2 ARCHER trial. In 2024, we initiated our Phase 3 ARCHER II trial, a global, sham-controlled, double-masked trial expected to enroll ~630 patients who have dry AMD with GA. The primary endpoint of ARCHER II is prevention of ≥15-letter loss of BCVA, and a secondary objective structural measure is prevention of ellipsoid zone (EZ) loss. The single-study program will be analyzed as two sub-studies for the U.S. in accordance with the FDA's two-trial recommendation. Accordingly, Annexon no longer plans to conduct a second injection-controlled head-to-head Phase 3 trial. We expect to complete enrollment of ARCHER II in the second half of 2025 and report topline data in the second half of 2026. ANX007 is the first and only therapeutic candidate for the treatment of GA to receive Priority Medicine, or PRIME, designation by the EMA, which provides early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options.

- **ANX1502 for Autoimmune Indications:** We are advancing ANX1502, a novel oral small molecule inhibitor of classical complement which we believe is first-in-kind. In a Phase 1 single-ascending dose, or SAD, and multiple-ascending dose, or MAD, clinical trial in healthy volunteers designed to evaluate the safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD, ANX1502 was generally well tolerated across cohorts with no serious adverse events, achieved target levels of active drug and showed supportive impact on a PD biomarker of complement activity that support its advancement. We are evaluating a tablet formulation of ANX1502 in an ongoing proof-of-concept study in patients with cold agglutinin disease, or CAD, to assess PK, PD and clinical efficacy endpoints (e.g., hemolysis as measured by reduction of elevated bilirubin) and data are expected in mid-2025. Following the successful completion of the proof-of-concept study, we intend to evaluate ANX1502 in a host of diseases, including serious complement-mediated autoimmune diseases, with the aim of providing enhanced efficacy and offering convenient dosing administration for long-term treatment of chronic conditions.

We were incorporated in March 2011 and commenced operations later that year. To date, we have focused primarily on performing research and development activities, hiring personnel and raising capital to support and expand these activities. We do not have any products approved for sale, and we have not generated any revenue from product sales. We have incurred net losses each year since our inception. Our net losses were $138.2 million and $134.2 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $710.7 million and cash and cash equivalents and short-term investments of $312.0 million.

Components of Operating Results

Revenue

Our product candidates are not approved for commercial sale. We have not generated any revenue from sales of our product candidates and do not expect to do so in the foreseeable future and until we complete clinical development, submit regulatory filings and receive approvals from applicable regulatory bodies for such product candidates, if ever.

Operating Expenses

Research and Development

Research and development expenses account for a significant portion of our operating expenses. Research and development expenses consist primarily of direct and indirect costs incurred for the development of our product candidates.

Direct expenses include:

- preclinical and clinical outside service costs associated with discovery, preclinical and clinical testing of our product candidates;
- professional services agreements with third party contract organizations, investigative clinical trial sites and consultants that conduct research and development activities on our behalf;
- contract manufacturing costs to produce clinical trial materials and commercial materials to support any BLA to the FDA; and
- laboratory supplies and materials.

Indirect expenses include:

- compensation and personnel-related expenses (including stock-based compensation);
- allocated expenses for facilities and depreciation; and
- other indirect costs.

We record research and development expenses as incurred. Payments made to other entities are under agreements that are generally cancelable by us. Advance payments for goods or services to be received in future periods for use in research and development activities are deferred as prepaid expenses. The prepaid amounts are then expensed as the related services are performed. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates.

We expect our future research and development expenses to increase as we pursue regulatory approval of our product candidates, continue to advance our product candidates through late-stage clinical trials, invest in capabilities to prepare for commercialization including manufacturing, and hire additional personnel to support our organization. The process of conducting the necessary clinical research, development and manufacturing to obtain regulatory approval is costly and time-consuming, and the successful development and approval of our product candidates is highly uncertain.

General and Administrative

General and administrative expenses consist primarily of compensation and personnel-related expenses (including stock-based compensation) for our personnel in executive, finance and other administrative functions. General and administrative expenses also include professional fees paid for accounting, legal and tax services, allocated expenses for facilities and depreciation and other general and administrative costs.

We expect our general and administrative expenses to increase as we continue to support our research and development activities, grow our business, advance our product candidates in late-stage clinical trials and toward regulatory approval and commercialization activities, and operate as a public company.

Interest and Other Income, Net

Interest and other income, net, primarily consists of interest income earned on our cash equivalents and short-term investments.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following tables summarize our results of operations for the periods presented:

	Year Ended December 31,		Dollar Change	% Change
	2024	2023		
	(in thousands)			
Operating expenses:				
Research and development	$ 119,448	$ 113,756	$ 5,692	5%
General and administrative	34,625	29,967	4,658	16%
Total operating expenses	154,073	143,723	10,350	7%
Loss from operations	(154,073)	(143,723)	(10,350)	7%
Interest and other income, net	15,873	9,486	6,387	67%
Net loss	$ (138,200)	$ (134,237)	$ (3,963)	3%

Research and Development Expenses

	Year Ended December 31,		Dollar Change	% Change
	2024	2023		
	(in thousands)			
Direct costs:				
Clinical and nonclinical outside services	$ 37,901	$ 41,456	$ (3,555)	(9%)
Contract manufacturing	20,328	22,598	(2,270)	(10%)
Consulting and professional services	17,083	8,347	8,736	105%
Laboratory supplies and materials	848	1,453	(605)	(42%)
Indirect costs:				
Compensation and personnel-related (including stock-based compensation)	35,492	33,868	1,624	5%
Facilities and depreciation	6,875	5,009	1,866	37%
Other	921	1,025	(104)	(10%)
Total research and development expenses	$ 119,448	$ 113,756	$ 5,692	5%

Research and development expenses increased by $5.7 million, or 5%, for the year ended December 31, 2024 compared to the year ended December 31, 2023. The increase was primarily due to an increase of $8.7 million in consulting and professional services in support of our development organization driving the advancement of our flagship programs, an increase of $1.9 million in facilities related costs due to the expiration of a sublease agreement, and an increase of $1.6 million in compensation and personnel-related expenses due to an increase in headcount, partially offset by a decrease of $3.6 million in direct clinical and nonclinical outside services costs due to completion of the Phase 2 ARCHER trial in GA in 2023, a decrease of $2.3 million due to timing of contract manufacturing expenses for ANX005, and a decrease of $0.6 million in laboratory supplies and materials.

General and Administrative Expenses

	Year Ended December 31,		Dollar Change	% Change
	2024	2023		
	(in thousands)			
Compensation and personnel-related (including stock-based compensation)	$ 16,858	$ 16,404	$ 454	3%
Consulting and professional services	13,161	9,738	3,423	35%
Facilities and depreciation	2,598	1,946	652	34%
Other	2,008	1,879	129	7%
Total general and administrative expenses	$ 34,625	$ 29,967	$ 4,658	16%

General and administrative expenses increased by $4.7 million, or 16%, for the year ended December 31, 2024 compared to the year ended December 31, 2023. The increase was primarily due to an increase of $3.4 million in consulting and professional services costs for business development, market research, and recruitment costs, an increase of $0.7 million in facilities related costs due to the expiration of a sublease agreement, and an increase in compensation and personnel-related expenses of $0.5 million due to an increase in headcount.

Interest and other income, net

Interest and other income increased by $6.4 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The increase was primarily due to higher average cash and investment balances and favorable interest rates.

Liquidity and Capital Resources

Sources of Liquidity

Due to our significant research and development expenditures, we have generated operating losses since our inception.

We have funded our operations primarily through the sale of equity securities. As of December 31, 2024, we had available cash and cash equivalents and short-term investments of $312.0 million and an accumulated deficit of $710.7 million.

Historical Cash Flows

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Net cash used in operating activities	$ (118,006)	$ (121,142)
Net cash (used in) provided by investing activities	(218,797)	70,703
Net cash provided by financing activities	161,206	135,524
(Decrease) increase in cash, cash equivalents and restricted cash	$ (175,597)	$ 85,085

Cash Flow from Operating Activities

Cash used in operating activities for the year ended December 31, 2024 was $118.0 million, which consisted of a net loss of $138.2 million, partially offset by $13.8 million in non-cash charges and a net change of $6.4 million in our operating assets and liabilities. The non-cash charges consisted of stock-based compensation of $19.4 million,

depreciation and amortization of $2.2 million, and reduction in the carrying amount of right-of-use assets of $1.3 million, partially offset by accretion of discount on available-for-sale securities of $9.1 million.

Cash used in operating activities for the year ended December 31, 2023 was $121.1 million, which consisted of a net loss of $134.2 million and a net change of $5.8 million in our operating assets and liabilities, partially offset by $18.9 million in non-cash charges. The non-cash charges consisted of stock-based compensation of $18.2 million, depreciation and amortization of $2.1 million, and reduction in the carrying amount of right-of-use assets of $1.1 million, partially offset by accretion of discount on available-for-sale securities of $2.6 million.

Cash Flow from Investing Activities

Cash used in investing activities for the year ended December 31, 2024 was $218.8 million, which consisted of $583.9 million of purchases of available-for-sale securities, partially offset by $365.1 million of proceeds from maturities of available-for-sale securities.

Cash provided by investing activities for the year ended December 31, 2023 was $70.7 million, which consisted of $179.0 million of proceeds from maturities of available-for-sale securities, partially offset by $108.1 million of purchases of available-for-sale securities and $0.2 million of equipment purchases.

Cash Flow from Financing Activities

Cash provided by financing activities for the year ended December 31, 2024 was $161.2 million, which consisted of $116.8 million of net proceeds from the issuance of common stock and pre-funded warrants under our 2024 financing, $42.8 million of net proceeds from the issuance of common stock under our 2021 and 2024 ATM programs and $1.6 million of proceeds from the exercise of common stock options and employee stock purchase plan purchases.

Cash provided by financing activities for the year ended December 31, 2023 was $135.5 million, which consisted of $117.5 million of net proceeds from the issuance of common stock and pre-funded warrants, $17.5 million of net proceeds from the issuance of common stock to a related party under our at-the-market offering program and $0.6 million of proceeds from the exercise of common stock options and employee stock purchase plan purchases.

Funding Requirements

We use our cash to fund operations, primarily to fund our clinical trials, research and development expenditures and related personnel costs. We expect our future research and development expenses to increase as we pursue regulatory approval of our product candidates, continue to advance our product candidates through late-stage clinical trials, invest in capabilities to prepare for commercialization including manufacturing, and hire additional personnel to support our organization. In addition, we expect our general and administrative expenses to increase as we continue to support our research and development activities, grow our business, advance our product candidates in late-stage clinical trials and toward regulatory approval and commercialization activities, and operate as a public company. The timing and amount of our operating expenditures will depend on many factors, including:

- the scope, progress, results and costs of researching and developing our current product candidates or any other future product candidates we choose to pursue, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining feedback from regulators on our clinical trials and regulatory approvals for our lead product candidates or any future product candidates;
- the number and characteristics of any additional product candidates we develop or acquire;
- the timing and amount of any milestone, royalty and/or other payments we are required to make pursuant to our current or any future license or collaboration agreements;
- the cost of manufacturing our lead product candidates or any future product candidates and any products we successfully commercialize;
- the cost of building a sales force in anticipation of product commercialization;

- the cost of commercialization activities of our product candidates, if approved for sale, including marketing, sales and distribution costs;
- our ability to establish strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract, hire and retain skilled personnel;
- the costs associated with operating as a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio; and
- the timing, receipt and amount of sales of any future approved products.

Based upon our current operating plan, we believe that our existing cash and cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2026. We will require substantial additional financing to achieve our goals, 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 programs, commercialization efforts or other operations. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. Until such time, if ever, as we can generate substantial product revenue, we will be required to seek additional funding in the future and currently intend to do so through public or private equity offerings or debt financings, credit or loan facilities, collaborations or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all. If we fail to obtain necessary capital when needed on acceptable terms, or at all, we could be forced to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

2024 Financing

In June 2024, we raised net proceeds of approximately $116.8 million after deducting underwriting discounts and offering expenses through the sale of 13,001,120 shares of our common stock, par value $0.001 per share at a price of $6.25 per share and pre-funded warrants to purchase an aggregate of 7,000,000 shares of common stock at a price of $6.249 per share, which equals the per share offering price for the shares of common stock less the $0.001 exercise price for each pre-funded warrant.

2023 Financing

In December 2023, we raised net proceeds of approximately $117.0 million after deducting underwriting discounts and offering expenses through the sale of 25,035,000 shares of our common stock, par value $0.001 per share at a price of $2.880 per share and pre-funded warrants to purchase an aggregate of 18,379,861 shares of common stock at a price of $2.879 per share, which equals the per share offering price for the shares of common stock less the $0.001 exercise price for each pre-funded warrant. We issued an aggregate of 5,243,400 and 965,427 shares of common stock upon cashless and cash exercise of these pre-funded warrants in February 2024 and April 2024, respectively.

2022 Financing

In July 2022, we raised net proceeds of approximately $122.5 million after deducting fees and expenses through the sale of an aggregate of 9,013,834 shares of common stock, pre-funded warrants to purchase up to 24,696,206 shares of our common stock and accompanying common warrants to purchase up to 8,427,508 shares of our common

stock. The offering price per share and accompanying common warrant was $3.87125 per share and the offering price per pre-funded warrant and accompanying common warrant was $3.87025 per share, which equals the per share offering price for the shares of common stock less the $0.001 exercise price for each such pre-funded warrant. The pre-funded warrants remain exercisable until exercised in full. The common warrants have an exercise price of $5.806875 per share and expire on June 30, 2025. Both the pre-funded and common warrants are immediately exercisable, subject to beneficial ownership limitations. We issued an aggregate of 2,582,557 shares of common stock upon the cashless exercise of the pre-funded warrants in March 2023. We issued an aggregate of 19,901 and 2,739,096 shares of common stock upon the cashless exercise of the common warrants and pre-funded warrants in June 2024 and November 2024, respectively.

Pre-Funded and Common Warrants

The following summarizes warrant activity during the years ended December 31, 2024 and 2023:

	Number of Common Warrants	Number of Pre-funded Warrants	Weighted-Average Exercise Price
Balances as of December 31, 2022	8,427,508	24,696,206	
Issued	—	18,379,861	$ 0.001
Exercised	—	(2,583,144)	$ 0.001
Balances as of December 31, 2023	8,427,508	40,492,923	
Issued	—	7,000,000	$ 0.001
Exercised	(322,893)	(8,949,346)	$ 0.216
Balances as of December 31, 2024	8,104,615	38,543,577	

2024 At-the-Market (ATM) Program

In March 2024, we entered into a sales agreement with Cowen and Company LLC, or TD Cowen, as sales agent, or 2024 ATM program, pursuant to which we may issue and sell shares of our common stock for an aggregate maximum offering of $100.0 million. TD Cowen is entitled to compensation up to 3% of the aggregate gross proceeds for the common stock sold through the 2024 ATM program. During the year ended December 31, 2024, we sold 750,000 shares of common stock for net proceeds of approximately $4.5 million, after deducting commissions paid to TD Cowen. As of December 31, 2024, approximately $95.4 million remained available for the offer and sale of shares of common stock under the 2024 ATM program.

2021 ATM Program

In August 2021, we entered into a sales agreement with TD Cowen, as sales agent, pursuant to which we may issue and sell shares of our common stock for an aggregate maximum offering of $100.0 million under an at-the-market offering program, or 2021 ATM program. TD Cowen is entitled to compensation up to 3% of the aggregate gross proceeds for the common stock sold through the 2021 ATM program. During the years ended December 31, 2024 and 2023, we sold 7,576,067 shares and 2,646,458 shares of common stock, respectively, under the 2021 ATM program for net proceeds of approximately $38.4 million and $17.5 million, respectively, after deducting commissions paid to TD Cowen and other financing costs. The Form S-3 registration statement, which registered the 2021 ATM Program, expired on August 15, 2024. As a result, no shares of common stock may be sold under the 2021 ATM Program.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions for the reported amounts of assets,

liabilities, expenses and related disclosures. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions and any such differences may be material.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Accrued and Prepaid Research and Development Costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include the conduct of clinical trials and nonclinical studies. We estimate preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions, clinical research organizations, and clinical manufacturing organizations that conduct and manage preclinical studies and clinical trials on our behalf. In recording service fees as either prepaid or accrued costs, we estimate the period over which services will be performed and the level of effort to be expended in each period. The level of judgment required to estimate research and development expenses varies based on the nature of the services being performed and the underlying support obtained. Accordingly, research and development expenses supported by invoices or reports of costs from third-party providers for the services performed do not require us to make significant estimates.

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services provided and efforts expended pursuant to contracts with contract research organizations that may be used to conduct and manage our clinical trials. We recognize costs for contract manufacturing based on evaluation of the progress to completion of specific tasks. These estimates of the expense are based on communications with and information provided by the third-party service providers at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the amounts recorded accordingly. The estimates are trued up to reflect the best information available at the time of the financial statement issuance. We have not experienced any material differences between accrued or prepaid costs and actual costs incurred since inception.

We defer and capitalize non-refundable advance payments for goods or services that will be used or rendered for future research and development activities as prepaid expenses until the related goods are delivered or services are performed. We evaluate such payments for current or long-term classification based on when such services are expected to be received.

Warrants

To assess the initial classification of our warrants as either liability or equity, we apply judgment when evaluating the potential settlement options. We first assess whether the warrants are within the scope of ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity, or* ASC 480. Under ASC 480, warrants are considered liability classified if the warrants are mandatorily redeemable, obligate us to settle the warrants or the underlying shares by paying cash or other assets, or require settlement by issuing variable number of shares.

If the warrants are not within the scope of ASC 480, they are subsequently assessed under ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock , or* ASC 815-40. We review the terms of the warrants to determine whether they require or may require us to settle or net settle the contract for cash which would result in classification of the warrants as liabilities recorded at fair value. If the warrants do not require liability classification under ASC 815-40, and in order to conclude equity classification, we also assess whether the warrants are indexed to our common stock and meet equity classification criteria under ASC 815-40. Liability-classified warrants require fair value accounting at issuance and subsequent to initial issuance with all changes in fair value after the issuance date recorded in the consolidated statements of operations. Equity-classified warrants only require fair value accounting at issuance and are not subsequently remeasured.

Our pre-funded and common warrants are equity-classified instruments that were recorded in additional paid-in capital at issuance and are not subject to remeasurement. We periodically evaluate changes in facts and circumstances that could impact the classification of warrants.

Recent Accounting Pronouncements Not Yet Adopted

See Note 2—Basis of Presentation and Significant Accounting Policies to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for information about recent accounting pronouncements, the timing of their adoption, and our assessment, to the extent we have made one yet, of their potential impact on our financial condition of results of operations.

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

Not required for the Company as a smaller reporting company.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors
Annexon, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Annexon, Inc. and subsidiary (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a 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.

Pre-funded warrants

As discussed in Note 6 to the consolidated financial statements, in June 2024 the Company closed a financing transaction which included the issuance of common stock and pre-funded warrants to purchase its common stock. Upon issuance, the pre-funded warrants were recorded at fair value as of the grant date as a component of stockholders' equity within additional paid-in capital.

We identified the balance sheet classification of the pre-funded warrants as part of the June 2024 financing transaction as either liabilities or equity as a critical audit matter. Subjective auditor judgment was required in the evaluation of the balance sheet classification of the pre-funded warrants due to certain provisions included within the warrant agreement.

The following are the primary procedures we performed to address this critical audit matter. We obtained and inspected the pre-funded warrant agreement to identify key terms and conditions within the agreement that were relevant to the balance sheet classification determination. We obtained and assessed the Company's technical accounting analysis to evaluate whether the Company had considered those key terms and conditions of the pre-funded warrant agreement. We evaluated the Company's interpretation and application of the relevant accounting literature, including considerations of the settlement provisions unique to the pre-funded warrants.

/s/ KPMG LLP

We have served as the Company’s auditor since 2016.

San Francisco, California
March 3, 2025

ANNEXON, INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2024	2023
Assets		
Current assets:		
Cash and cash equivalents	$ 49,498	$ 225,110
Short-term investments	262,519	34,606
Prepaid expenses and other current assets	4,444	4,144
Total current assets	316,461	263,860
Restricted cash	1,032	1,032
Property and equipment, net	12,638	14,773
Operating lease right-of-use assets	16,705	18,009
Other non-current assets	3,235	—
Total assets	$ 350,071	$ 297,674
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 10,426	$ 5,487
Accrued and other current liabilities	17,568	10,276
Operating lease liabilities, current	2,518	2,165
Total current liabilities	30,512	17,928
Operating lease liabilities, non-current	26,454	29,190
Total liabilities	56,966	47,118
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Common stock, $0.001 par value; 300,000,000 shares authorized as of December 31, 2024 and 2023; 109,381,556 and 78,369,099 shares issued and outstanding as of December 31, 2024 and 2023, respectively	109	78
Additional paid-in capital	1,003,685	823,029
Accumulated other comprehensive income (loss)	10	(52)
Accumulated deficit	(710,699)	(572,499)
Total stockholders' equity	293,105	250,556
Total liabilities and stockholders' equity	$ 350,071	$ 297,674

See accompanying notes to consolidated financial statements.

ANNEXON, INC.
Consolidated Statements of Operations
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2024	2023
Operating expenses:		
Research and development	$ 119,448	$ 113,756
General and administrative	34,625	29,967
Total operating expenses	154,073	143,723
Loss from operations	(154,073)	(143,723)
Interest and other income, net	15,873	9,486
Net loss	$ (138,200)	$ (134,237)
Net loss per share, basic and diluted	$ (1.01)	$ (1.77)
Weighted-average shares used in computing net loss per share, basic and diluted	137,404,145	75,673,081

See accompanying notes to consolidated financial statements.

ANNEXON, INC.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,	
	2024	2023
Net loss	$ (138,200)	$ (134,237)
Other comprehensive income (loss):		
Foreign currency translation adjustment	(15)	5
Unrealized gain on available-for-sale securities	77	315
Comprehensive loss	$ (138,138)	$ (133,917)

See accompanying notes to consolidated financial statements.

ANNEXON, INC.
Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Cost				
Balances as of December 31, 2022	47,722,995	$ 48	$ 669,780	$ (372)	$ (438,262)	$ 231,194
Exercise of stock options	76,888	—	145	—	—	145
Exercise of pre-funded warrants	2,582,557	3	(3)	—	—	—
Issuance of common stock to a related party, net of issuance costs of $525	2,646,458	2	17,468	—	—	17,470
Issuance of common stock and pre-funded warrants, net of issuance cost of $8,014	25,035,000	25	116,977	—	—	117,002
Issuance of common stock per Employee Stock Purchase Plan purchase	133,105	—	479	—	—	479
Restricted stock vested in the period	172,096	—	—	—	—	—
Stock-based compensation	—	—	18,183	—	—	18,183
Other comprehensive income	—	—	—	320	—	320
Net loss	—	—	—	—	(134,237)	(134,237)
Balances as of December 31, 2023	78,369,099	78	823,029	(52)	(572,499)	250,556
Exercise of stock options	382,122	—	1,232	—	—	1,232
Exercise of pre-funded warrants	8,947,923	9	(9)	—	—	—
Exercise of common warrants	19,901	—	—	—	—	—
Issuance of common stock, net of issuance costs of $1,528	8,326,067	8	42,835	—	—	42,843
Issuance of common stock and pre-funded warrants, net of issuance costs $8,183	13,001,120	13	116,804	—	—	116,817
Issuance of common stock per Employee Stock Purchase Plan purchase	138,147	1	361	—	—	362
Restricted stock vested in the period	197,177	—	—	—	—	—
Stock-based compensation	—	—	19,433	—	—	19,433
Other comprehensive income	—	—	—	62	—	62
Net loss	—	—	—	—	(138,200)	(138,200)
Balances as of December 31, 2024	109,381,556	$ 109	$ 1,003,685	$ 10	$ (710,699)	$ 293,105

See accompanying notes to consolidated financial statements.

ANNEXON, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2024	2023
Operating activities:		
Net loss	$ (138,200)	$ (134,237)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,150	2,148
Accretion of discount on available-for-sale securities	(9,054)	(2,550)
Stock-based compensation	19,433	18,183
Reduction in the carrying amount of right-of-use assets	1,304	1,119
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(300)	1,352
Other non-current assets	(3,184)	—
Accounts payable	4,936	(2,077)
Accrued and other current liabilities	7,292	(3,577)
Operating lease liabilities	(2,383)	(1,503)
Net cash used in operating activities	(118,006)	(121,142)
Investing activities:		
Purchases of property and equipment	(15)	(193)
Purchases of available-for-sale securities	(583,932)	(108,088)
Proceeds from maturities of available-for-sale securities	365,150	178,984
Net cash (used in) provided by investing activities	(218,797)	70,703
Financing activities:		
Proceeds from the exercise of common stock options	1,232	90
Proceeds from Employee Stock Purchase Plan purchases	362	479
Proceeds from the issuance of common stock, including to related parties, of zero and $17,995 for the years ended December 31, 2024 and 2023, respectively	44,371	17,995
Proceeds from the issuance of common stock and pre-funded warrants, net of commissions	117,500	117,515
Payment of financing costs	(2,259)	(555)
Net cash provided by financing activities	161,206	135,524
(Decrease) increase in cash, cash equivalents and restricted cash	(175,597)	85,085
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(15)	5
Cash, cash equivalents and restricted cash		
Beginning of period	226,142	141,052
End of period	$ 50,530	$ 226,142
Supplemental disclosure of cash flow information:		
Cash paid for amounts included in the measurement of lease liability	$ 4,893	$ 4,728
Non-cash investing and financing activities:		
Deferred offering costs included in accounts payable and accrued liabilities	$ 3	$ 483
Deferred offering costs included in other non-current assets	$ 51	$ —
Purchases of property and equipment included in accounts payable and accrued liabilities	$ —	$ —

See accompanying notes to consolidated financial statements.

ANNEXON, INC.
Notes to Consolidated Financial Statements

1. Organization

Annexon, Inc., or the Company, is a clinical-stage biopharmaceutical company pioneering a new class of complement medicines for people living with devasting inflammatory-related diseases. The Company is located in Brisbane, California and was incorporated in Delaware in March 2011.

The Company's wholly-owned subsidiary, Annexon Biosciences Australia Pty Ltd, or the Subsidiary, is a proprietary limited company incorporated in 2016 and domiciled in Australia.

Liquidity

Since inception, the Company has been involved primarily in performing research and development activities, conducting clinical trials, hiring personnel, and raising capital to support and expand these activities. The Company has experienced losses and negative cash flows from operations since its inception and, as of December 31, 2024, had an accumulated deficit of $710.7 million and cash and cash equivalents and short-term investments of $312.0 million.

The Company has historically funded its operations through the issuance of shares of its common stock and warrants. Based on projected activities, management projects that existing cash and cash equivalents and short-term investments will enable the Company to fund its operating expenses and capital expenditure requirements for at least twelve months from the date of issuance of these financial statements. The Company's future viability beyond that point is dependent on its ability to achieve development milestones and obtain additional funding. Management expects to continue to incur losses and negative cash flows from operations for at least the next several years. There are uncertainties associated with the Company's ability to (1) obtain additional equity or debt financing on terms that are favorable to the Company, (2) enter into collaborative agreements with strategic partners, and (3) succeed in its future operations. If the Company is not able to obtain the required funding for its operations or is not able to obtain funding on terms that are favorable to the Company, it could be forced to delay, reduce or eliminate its research and development programs and its business could be materially harmed.

2. Basis of Presentation and Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America, or GAAP, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported expenses during the reporting period. Management evaluates its estimates, including but not limited to the fair value of investments, operating lease right-of-use assets and liabilities, valuation of deferred tax assets and uncertain tax positions (including valuation allowance), clinical trial accruals and stock-based compensation. The Company evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could differ from those estimates.

Principles of Consolidation

The consolidated financial statements include the operations of Annexon, Inc. and its wholly owned subsidiary and include the results of operations and cash flows of these entities. All intercompany balances and transactions have been eliminated in consolidation.

Segments

The Company's chief operating decision maker ("CODM") is its Chief Executive Officer. The CODM reviews financial information on an aggregate basis for the purposes of evaluating financial performance and allocating the Company's resources. Accordingly, the Company has determined that it operates in one segment.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid instruments with an original maturity of three months or less at time of purchase to be cash equivalents. Cash equivalents, which includes amounts invested in money market funds and short-term government bonds, are stated at fair value.

Restricted cash as of December 31, 2024 relates to the letters of credit established for the Company's office lease.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the same amounts shown in the consolidated statements of cash flows (in thousands):

	December 31,	
	2024	2023
Cash	$ 2,651	$ 8,488
Cash equivalents	46,847	216,622
Cash and cash equivalents	49,498	225,110
Restricted cash	1,032	1,032
Cash, cash equivalents and restricted cash	$ 50,530	$ 226,142

Short-Term Investments

Short-term investments have been classified as available-for-sale and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. The Company determines the appropriate classification of its investments in debt securities at the time of purchase. Available-for-sale securities with original maturities beyond three months at the date of purchase are classified as current based on their availability for use in current operations.

The Company evaluates, on a quarterly basis, its available-for-sale debt securities for potential impairment. For available-for-sale debt securities in an unrealized loss position, the Company assesses whether such declines are due to credit loss based on factors such as changes to the rating of the security by a ratings agency, market conditions and supportable forecasts of economic and market conditions, among others. If credit loss exists, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any available-for-sale debt security before recovery of its amortized cost basis. If either condition is met, the security's amortized cost basis is written down to fair value and is recognized through interest and other income (expense), net. If neither condition is met, declines as a result of credit losses, if any, are recognized as an allowance for credit loss, limited to the amount of unrealized loss, through interest and other income (expense), net. Any portion of the unrealized loss that is not a result of a credit loss, is recognized in other comprehensive income (loss). Realized gains and losses, if any, on available-for-sale debt securities are included in interest and other income (expense), net.

The cost of investments sold is based on the specific-identification method. Interest on available-for-sale debt securities is included in interest and other income (expense), net.

Property and Equipment, Net

Property and equipment are carried at cost less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets. Depreciation begins at the time the asset is placed in service. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is reflected in operations in the period realized.

The useful lives of the property and equipment are as follows:

Computer equipment	3 years
Lab equipment and furniture and fixtures	5 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows the asset is expected to generate over its remaining life. When indications of impairment are present and the estimated undiscounted future cash flows from the use of these assets is less than the assets' carrying value, the related assets will be written down to fair value. There were no impairments of the Company's long-lived assets for the periods presented.

Leases

The Company determines if an arrangement is a lease at inception. The Company includes operating leases in operating lease right of use, or ROU, assets, current and noncurrent operating lease liabilities in the Company's consolidated balance sheets. The ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. The Company measures the ROU assets based on the associated lease liabilities adjusted for any lease incentives such as tenant improvement allowances. As most of the leases do not provide an implicit rate, the Company generally uses its incremental borrowing rate based on the estimated rate of interest for collateralized borrowing over a similar term of the lease payments at the commencement date. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise the option. Lease expense for lease payments is recognized on a straight-line basis, net of sublease income, over the lease term.

As a practical expedient, the Company elected, for all facility leases, not to separate non-lease components from lease components and instead to account for each separate lease component and its associated non-lease components as a single lease component. The Company elected to exclude from its balance sheets recognition of leases having a term of 12 months or less (short-term leases).

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carry forwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Valuation allowances are established when necessary to reduce deferred taxes to the amounts expected to be realized.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merit, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Commitments and Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. Legal costs incurred in connection with loss contingencies are expensed as incurred.

Warrants

Warrants are accounted for as either derivative liabilities or as equity instruments depending on the specific terms of the agreement. The Company's pre-funded and common warrants are equity-classified instruments that were recorded in additional paid-in capital at issuance and are not subject to remeasurement. The Company periodically evaluates changes in facts and circumstances that could impact the classification of warrants.

Research and Development Expense

Research and development expenses consist primarily of direct and indirect costs incurred for the development of the Company's product candidates.

Direct expenses include (i) preclinical and clinical outside service costs associated with discovery, preclinical and clinical testing of the Company's product candidates; (ii) professional services agreements with third-party contract organizations, investigative clinical trial sites and consultants that conduct research and development activities on the Company's behalf; (iii) contract manufacturing costs to produce clinical trial materials and commercial materials to support future biologics license applications ("BLA") to the FDA, and (iv) laboratory supplies and materials. Indirect expenses include (A) compensation and personnel-related expenses (including stock-based compensation), (B) allocated expenses for facilities and depreciation; and (C) other indirect costs.

Research and development costs are expensed as incurred. Payments made to third parties are under agreements that are generally cancelable by the Company. Advance payments for research and development activities are deferred as prepaid expenses. The prepaid amounts are expensed as the related services are performed.

The Company estimates preclinical studies and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on the Company's behalf. The Company also estimates manufacturing costs based on services performed pursuant to contracts with contract manufacturing organizations that develop and manufacture product on the Company's behalf. In accruing service fees, the Company estimates the period over which services will be performed and the level of effort to be expended in each period. These estimates are based on the Company's communications with the third-party service providers and on information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies significantly from the estimate, the Company will adjust the accrual accordingly to reflect the best information available at the time of the financial statement issuance. The Company has not experienced any material differences between accrued costs and actual costs incurred since its inception.

Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees and non-employee directors and consultants using a fair value method which requires the recognition of compensation expense for costs related to all stock-based payments, including stock options and restricted stock units, or RSUs. The fair value method requires the Company to estimate the fair value of stock options to employees and non-employees on the date of grant using the Black-Scholes option pricing model. The fair value of RSU awards is based on the fair value of the underlying common stock as of the grant date.

Stock-based compensation costs are based on the fair value of the underlying RSUs and options and recognized as expense on a straight-line basis over the requisite service period, which is the vesting period.

Determining the appropriate fair value model and related assumptions requires judgment, including estimating expected term, expected stock price volatility, risk-free interest rate and dividend yield. The Company accounts for forfeitures as they occur.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding for the period, without consideration for potential dilutive shares of common stock. As the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share because the effects of potentially dilutive securities are antidilutive.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents and short-term investments. The Company's cash and cash equivalents and short-term investments are held by high credit quality financial institutions in the United States. At times, such deposits may be in excess of the Federal Depository Insurance Corporation insured limits. Management believes that the financial institutions are financially sound, and accordingly, minimal credit risk exists with respect to the financial institutions.

Recently Adopted Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update (ASU) 2023-07, *Segment Reporting: Improvements to Reportable Segment Disclosures*, which requires disclosure of incremental segment information on an interim and annual basis. This ASU is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal periods beginning after December 15, 2024, and requires retrospective application to all prior periods presented in the financial statements. The Company adopted annual and interim requirements under ASU 2023-07 on January 1, 2024 and 2025, respectively. The adoption of ASU 2023-07 did not have a material impact on the Company's consolidated financial statements. See Note 10—*Segment Reporting.*

Recently Issued Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09, *Income Taxes: Improvements to Income Tax Disclosures*, which requires enhanced annual disclosures regarding the rate reconciliation and income taxes paid information. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024 and may be adopted on a prospective or retrospective basis. Early adoption is permitted. The Company is evaluating the impact of this guidance on its consolidated financial statements and related disclosures.

In November 2024, the FASB issued ASU 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures*: *Disaggregation of Income Statement Expenses*, which requires public entities to disclose additional information about specific expense categories in the notes to the financial statements on an interim and annual basis. This guidance is effective for annual reporting periods beginning after December 15, 2026, and interim periods beginning after December 15, 2027. Early adoption is permitted. The Company is currently evaluating the impact of this guidance on its consolidated financial statements.

3. Fair Value Measurements

The Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible. The Company determines fair value based on assumptions that market participants would use in pricing an asset or liability in the principal or most advantageous market. When considering market participant assumptions in fair value measurements, the following fair value hierarchy distinguishes between observable and unobservable inputs, which are categorized in one of the following levels:

- *Level 1 Inputs:* Unadjusted quoted prices in active markets for identical assets or liabilities accessible to the reporting entity at the measurement date.
- *Level 2 Inputs:* Other than quoted prices included in Level 1 inputs that are observable for the asset or

liability, either directly or indirectly, for substantially the full term of the asset or liability.

- *Level 3 Inputs:* Unobservable inputs for the asset or liability used to measure fair value to the extent that observable inputs are not available, thereby allowing for situations in which there is little, if any, market activity for the asset or liability at measurement date.

On a recurring basis, the Company measures certain financial assets and liabilities at fair value. The following tables summarize the fair value of the Company's financial assets and liabilities measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

		December 31, 2024			
	Valuation Hierarchy	Amortized Cost	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Aggregate Fair Value
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 31,680	$ —	$ —	$ 31,680
Government bonds	Level 2	15,167	—	—	15,167
Total cash equivalents		46,847	—	—	46,847
Short-term investments:					
Government bonds	Level 2	262,424	98	(3)	262,519
Total short-term investments		262,424	98	(3)	262,519
		$ 309,271	$ 98	$ (3)	$ 309,366

		December 31, 2023			
	Valuation Hierarchy	Amortized Cost	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Aggregate Fair Value
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 143,933	$ —	$ —	$ 143,933
Government bonds	Level 2	72,689	—	—	72,689
Total cash equivalents		216,622	—	—	216,622
Short-term investments:					
Government bonds	Level 2	34,596	10	—	34,606
Total short-term investments		34,596	10	—	34,606
		$ 251,218	$ 10	$ —	$ 251,228

All of the investments held as of December 31, 2024 had original maturities of less than two years. As of December 31, 2024, all of the investments are scheduled to mature in 12 months. During the year ended December 31, 2024, the Company did not recognize any credit losses. The Company determined that the decline in fair value of debt securities was not due to credit-related factors, and no allowance for expected credit losses was recorded as of December 31, 2024. There were nominal unrealized losses as of December 31, 2024, and no unrealized losses have been in the loss position for more than 12 months. However, the Company is planning to hold these securities until maturity and expects to recover the amortized cost basis.

For the years ended December 31, 2024 and 2023, the Company recognized no material realized gains or losses on financial instruments.

4. Balance Sheet Components

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2024	2023
Prepaid research and development costs	$ 2,640	$ 2,617
Prepaid insurance	700	704
Prepaid and other current assets	1,104	823
Total prepaid expenses and other current assets	$ 4,444	$ 4,144

Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2024	2023
Leasehold improvements	$ 17,254	$ 17,245
Laboratory equipment	1,838	1,832
Furniture and fixtures	692	692
Computer equipment and software	33	33
Total property and equipment, gross	19,817	19,802
Less: accumulated depreciation	(7,179)	(5,029)
Total property and equipment, net	$ 12,638	$ 14,773

Total depreciation expense recognized for the years ended December 31, 2024 and 2023 was $2.2 million and $2.1 million, respectively.

Accrued and Other Current Liabilities

Accrued and other current liabilities consisted of the following (in thousands):

	December 31,	
	2024	2023
Accrued research and development expenses	$ 10,992	$ 4,027
Accrued compensation	5,833	5,607
Accrued professional services	602	501
Other accrued and current liabilities	141	141
Total accrued and other current liabilities	$ 17,568	$ 10,276

5. Commitments and Contingencies

Leases

The Company leases its offices and laboratory in Brisbane, California, or the Brisbane Lease, under a ten-year noncancelable lease agreement that ends in October 2031 with a ten-year renewable option. In November 2021, the Company subleased unoccupied space for two years from December 2021 through November 2023, for aggregate sublease payments of $3.4 million. The sublease income, while it reduces the rent expense, is not considered in the value of the right-of-use assets or lease liabilities. The Company's sublease income was zero and $2.0 million for the years ended December 31, 2024 and 2023, respectively.

As of December 31, 2024, the operating lease right-of-use assets were $16.7 million and lease liabilities were $29.0 million in the consolidated balance sheet. The weighted average remaining lease term is 6.8 years.

The weighted average incremental borrowing rate used to measure the operating lease liability is 8.4%.

Operating lease cost for the years ended December 31, 2024 and 2023 was $3.8 million and $2.3 million, respectively. Variable lease payments for the years ended December 31, 2024 and 2023 were $2.3 million and $1.5 million, respectively.

Future minimum lease payments and related lease liabilities as of December 31, 2024 were as follows:

	(in thousands)
2025	$ 5,065
2026	5,242
2027	5,425
2028	5,615
2029 and thereafter	16,985
Total undiscounted lease payments	38,332
Less: Imputed interest	(9,360)
Total	$ 28,972

Guarantees and Indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2024, the Company did not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

6. Stockholders' Equity

2024 Financing

In June 2024, the Company raised net proceeds of approximately $116.8 million after deducting underwriting discounts and offering expenses through the sale of 13,001,120 shares of the Company's common stock, par value $0.001 per share at a price of $6.25 per share and pre-funded warrants to purchase an aggregate of 7,000,000 shares of common stock at a price of $6.249 per share, which equals the per share offering price for the shares of common stock less the $0.001 exercise price for each pre-funded warrant. The pre-funded warrants are immediately exercisable, subject to certain beneficial ownership limitations. The warrants meet the criteria for equity classification and were therefore recorded at fair value as of the grant date as a component of stockholders' equity within additional paid-in capital.

2023 Financing

In December 2023, the Company raised net proceeds of approximately $117.0 million after deducting underwriting discounts and offering expenses through the sale of 25,035,000 shares of the Company's common stock, par value $0.001 per share at a price of $2.880 per share and pre-funded warrants to purchase an aggregate of 18,379,861 shares of common stock at a price of $2.879 per share, which equals the per share offering price for the shares of common stock less the $0.001 exercise price for each pre-funded warrant. An entity related to one of the Company's directors participated in the public offering and purchased 350,000 shares of common stock for an aggregate price of approximately $1.0 million. The warrants meet the criteria for equity classification and were therefore recorded at fair value as of the grant date as a component of stockholders' equity within additional paid-in capital. The Company issued an aggregate of 5,243,400 shares and 965,427 shares of common stock upon the cashless and cash exercise of these pre-funded warrants in February 2024 and April 2024, respectively.

2022 Financing

In July 2022, the Company raised net proceeds of approximately $122.5 million after deducting fees and expenses through the sale of an aggregate of 9,013,834 shares of common stock, pre-funded warrants to purchase up to 24,696,206 shares of its common stock and accompanying common warrants to purchase up to 8,427,508 shares of its common stock. The offering price per share and accompanying common warrant was $3.87125 per share and the offering price per pre-funded warrant and accompanying common warrant was $3.87025 per share, which equals the per share offering price for the shares of common stock less the $0.001 exercise price for each such pre-funded warrant. The pre-funded warrants remain exercisable until exercised in full. The common warrants have an exercise price of $5.806875 per share and expire on June 30, 2025. Both the pre-funded and common warrants are immediately exercisable, subject to beneficial ownership limitations. The warrants meet the criteria for equity classification and were therefore recorded at fair value as of the grant date as a component of stockholders' equity within additional paid-in capital. The Company issued an aggregate of 2,582,557 shares of common stock upon the cashless exercise of the pre-funded warrants in March 2023. The Company issued an aggregate of 19,901 and 2,739,096 shares of common stock upon the cashless exercise of the common warrants and pre-funded warrants in June 2024 and November 2024, respectively.

Pre-Funded and Common Warrants

The following summarizes warrant activity during the years ended December 31, 2024 and 2023:

	Number of Common Warrants	Number of Pre-funded Warrants	Weighted-Average Exercise Price
Balances as of December 31, 2022	8,427,508	24,696,206	
Issued	—	18,379,861	$ 0.001
Exercised	—	(2,583,144)	$ 0.001
Balances as of December 31, 2023	8,427,508	40,492,923	
Issued	—	7,000,000	$ 0.001
Exercised	(322,893)	(8,949,346)	$ 0.216
Balances as of December 31, 2024	8,104,615	38,543,577	

2024 At-the-Market ("ATM") Program

In March 2024, the Company entered into a sales agreement with TD Cowen, as sales agent, or 2024 ATM program, pursuant to which the Company may issue and sell shares of its common stock for an aggregate maximum offering of $100.0 million. TD Cowen is entitled to compensation up to 3% of the aggregate gross proceeds for the common stock sold through the 2024 ATM program. During the year ended December 31, 2024, the Company sold 750,000 shares of common stock for net proceeds of approximately $4.5 million, after deducting commissions paid to TD Cowen. As of December 31, 2024, approximately $95.4 million remained available for the offer and sales of shares of common stock under the 2024 ATM program.

2021 ATM Program

In August 2021, the Company entered into a sales agreement with TD Cowen as sales agent, pursuant to which the Company may issue and sell shares of its common stock for an aggregate maximum offering of $100.0 million under an at-the-market offering program, or 2021 ATM program. TD Cowen is entitled to compensation up to 3% of the aggregate gross proceeds for the common stock sold through the 2021 ATM program. During the years ended December 31, 2024 and 2023, the Company sold 7,576,067 shares and 2,646,458 shares of common stock, respectively, under the 2021 ATM program for net proceeds of approximately $38.4 million and $17.5 million, respectively, after deducting commissions paid to TD Cowen and other financing costs. The Form S-3 registration statement, which registered the 2021 ATM Program, expired on August 15, 2024. As a result, no further shares of common stock may be sold under the 2021 ATM Program.

Common Stock

The holders of the Company's common stock have one vote for each share of common stock. Common stockholders are entitled to dividends when, as, and if declared by the board of directors. The holders have no preemptive or other subscription rights and there are no redemption or sinking fund provisions with respect to such shares. As of December 31, 2024, no dividends had been declared by the board of directors.

The Company reserved the following shares of common stock for issuance as follows:

	December 31,	
	2024	2023
Stock options issued and outstanding	14,594,720	9,208,970
Stock options reserved for 2020 Incentive Award Plan	2,109,758	1,988,340
Unvested restricted stock units outstanding	770,028	495,579
Common stock reserved for 2021 ATM program	—	2,619,471
Common stock reserved for 2024 ATM program	24,250,000	—
Common stock reserved for Employee Stock Purchase Plan	1,983,924	1,338,381
Common stock reserved for 2022 Employment Inducement Award Plan	3,359,230	758,084
Common stock reserved for pre-funded warrants	38,543,577	40,493,510
Common stock reserved for common warrants	8,104,615	8,427,508
Total common stock reserved	93,715,852	65,329,843

7. Equity Incentive Plan

In July 2020, the Company's board of directors and stockholders adopted and approved the 2020 Incentive Award Plan, or the 2020 Plan, and the Employee Stock Purchase Plan, or the ESPP, which became effective in connection with the IPO.

The Company may not grant any additional awards under the 2011 Equity Incentive Plan, or the 2011 Plan. The 2011 Plan will continue to govern outstanding equity awards granted thereunder.

2020 Equity Incentive Plan

The number of shares of common stock reserved for issuance under the 2020 Plan automatically increase on the first day of January, in an amount equal to 4% of the total number of shares of the Company's capital stock outstanding on the last day of the preceding year, or a lesser number of shares determined by the Company's board of directors.

Awards granted under the 2020 Plan expire no later than ten years from the date of grant. For the Incentive Stock Options, or ISOs, and Nonstatutory Stock Options, or NSOs, the option price shall not be less than 100% of the estimated fair value on the date of grant. Options granted typically vest over a four-year period but may be granted with different vesting terms. As of December 31, 2024 and 2023, there were 2,109,758 and 1,988,340 shares available for issuance under the 2020 Plan, respectively.

2022 Employment Inducement Award Plan

In July 2022, the Company's board of directors adopted the Annexon, Inc. 2022 Employment Inducement Award Plan, or the Inducement Plan, and together with the 2011 Plan and the 2020 Plan, the Plans. The Inducement Plan was adopted by the Company's board of directors without stockholder approval pursuant to Nasdaq Marketplace Rule 5635(c)(4), or Rule 5635(c)(4). In accordance with Rule 5635(c)(4), awards made under the Inducement Plan may only be granted to newly hired employees as an inducement material to the employees entering into employment with the Company. Awards granted under the Inducement Plan expire no later than ten years from the date of grant. An aggregate of 7,850,000 shares of common stock were reserved for issuance under the Inducement Plan. As of December 31, 2024 and 2023, there were 3,359,230 and 758,084 shares available for issuance under the Inducement Plan, respectively.

Stock options

The following table presents stock option activity under the Plans for the period:

	Number of Shares	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balances as of December 31, 2023	9,208,970	$ 10.31	7.53	$ 2,930
Stock options granted	6,749,824	$ 5.73		
Stock options exercised	(382,122)	$ 3.22		
Stock options forfeited	(981,952)	$ 11.55		
Balances as of December 31, 2024	14,594,720	$ 8.29	7.94	$ 4,059
Vested and Exercisable as of December 31, 2024	6,813,637	$ 11.06	6.58	$ 2,194

The total intrinsic value of options exercised during the years ended December 31, 2024 and 2023 was $1.2 million and $0.3 million, respectively. The intrinsic value is the difference between the fair value of the Company's common stock at the time of exercise and the exercise price of the stock option.

The weighted-average grant date fair value of options granted to employees during the years ended December 31, 2024 and 2023 was $4.56 and $3.72 per share, respectively.

As of December 31, 2024, the total unrecognized stock-based compensation cost related to outstanding unvested stock options was $33.1 million, which the Company expects to recognize over an estimated weighted-average period of 3.0 years.

Restricted Stock Units

RSUs are share awards that entitle the holder to receive freely tradeable shares of the Company's common stock upon vesting. The RSUs cannot be transferred and the awards are subject to forfeiture if the holder's employment terminates prior to the release of the vesting restrictions. The RSUs generally vest over a three-year period in equal amounts on an annual basis, provided the employee remains continuously employed with the Company. The fair value of the RSUs is equal to the closing price of the Company's common stock on the grant date.

A summary of RSU activity under the equity incentive plan and related information is as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value Per Share
Unvested as of December 31, 2023	495,579	$ 5.69
Granted	602,600	5.13
Vested	(197,177)	5.85
Cancelled	(130,974)	5.29
Unvested as of December 31, 2024	770,028	$ 5.28

As of December 31, 2024, unrecognized stock-based compensation expense related to outstanding unvested RSUs was $2.5 million, which is expected to be recognized over a weighted-average period of 1.9 years.

Employee Stock Purchase Plan

The ESPP enables eligible employees to purchase shares of the Company's common stock at the end of each offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower. Eligible employees generally included all employees. Share purchases are funded through payroll deductions of at least 1%, and up to 15% of an employee's eligible compensation for each payroll period. The number of shares reserved for issuance under the ESPP increase automatically on the first

day of each fiscal year, by a number equal to, 1% of the shares of common stock outstanding on the last day of the immediately preceding fiscal year, or such number of shares determined by the Company's board of directors. As of December 31, 2024, 1,983,924 shares were available for future purchase. The ESPP generally provides for six-month consecutive offering periods beginning on May 15th and November 15th of each year. The ESPP is a compensatory plan as defined by the authoritative guidance for stock compensation. As such, stock-based compensation expense has been recorded for the years ended December 31, 2024 and 2023.

The stock-based compensation expense related to the ESPP for the years ended December 31, 2024 and 2023 was $0.2 million and $0.3 million, respectively.

Stock-Based Compensation Expense

The total stock-based compensation expense recognized was as follows (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development	$ 9,670	$ 8,878
General and administrative	9,763	9,305
Total stock-based compensation expense	$ 19,433	$ 18,183

To determine the value of stock option awards for stock-based compensation purposes, the Company uses the Black-Scholes option pricing model and the assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment.

Fair Value of Common Stock—The fair value of each share of underlying common stock is based on the closing price of the Company's common stock as reported on the date of grant on the Nasdaq Global Select Market.

Expected Term—The expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company continues using the simplified method as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term due to the limited period of time its equity shares have been publicly traded.

Expected Volatility—Beginning in 2024, the expected volatility was estimated based on a weighted volatility using both the Company's trading history for its common stock and the average volatility for comparable publicly traded life sciences companies over a period equal to the expected term of the stock option grants. Prior to 2024, the expected volatility was estimated based on the average volatility for comparable publicly traded life sciences companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on the similar size, stage in life cycle or area of specialty.

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

Dividend Yield—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of each stock option issued was estimated on the date of grant using the Black-Scholes option pricing model with the following assumptions:

	Year Ended December 31,	
	2024	2023
Expected term (in years)	5.50 - 6.08	5.50 - 6.08
Expected volatility	95.90% - 99.80%	81.20% - 82.40%
Risk-free interest rate	3.48% - 4.65%	3.47% - 4.85%
Dividend yield	—	—

8. Income Taxes

For financial reporting purposes, loss before provision for income taxes, includes the following components (in thousands):

	Year Ended December 31,	
	2024	2023
Domestic	$ (138,193)	$ (134,233)
Foreign	(7)	(4)
Loss before income taxes	$ (138,200)	$ (134,237)

For each of the years ended December 31, 2024 and 2023, the Company incurred insignificant amounts for an income tax provision. The U.S. federal and California deferred tax assets generated from the Company's net operating losses have been fully reserved, as the Company believes it is not more likely than not that the benefit will be realized.

Reconciliation of income tax computed at federal statutory rates to the reported provision for income taxes was as follows (in thousands):

	Year Ended December 31,	
	2024	2023
Tax provision at U.S. statutory rate	$ (29,022)	$ (28,190)
Stock-based compensation	1,548	1,343
Research and development tax credits	(9,526)	(3,883)
Change in valuation allowance	35,184	29,066
Section 162(m) compensation	1,773	1,594
Other	43	70
Provision for income taxes	$ —	$ —

Deferred Tax Assets and Liabilities

The tax effects of temporary differences that give rise to significant portions of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2024	2023
Deferred Tax Assets:		
Net operating loss carryforwards	$ 94,198	$ 70,996
Research and development credits	29,095	16,070
Other intangibles	5	3
Accruals and reserves	1,116	1,074
Stock-based compensation	5,599	5,185
Capitalized research and development	49,837	36,568
Lease liabilities	6,087	6,610
Total gross deferred tax assets	185,937	136,506
Less: valuation allowance	(180,958)	(130,939)
Total deferred tax assets, net	$ 4,979	$ 5,567
Deferred Tax Liabilities:		
Fixed assets	$ (1,469)	$ (1,771)
Right-of-use assets	(3,510)	(3,796)
Total gross deferred tax liabilities	(4,979)	(5,567)
Net deferred tax assets	$ —	$ —

During 2024, the Company completed a research credit study for the years ended December 31, 2020 through 2023. This resulted in true ups to the credit carryovers, which also impacted the Section 174 capitalized research expenses and net operating losses deferred tax assets disclosed.

As of December 31, 2024, the Company had $367.7 million of federal and $223.8 million of state net operating loss, or NOL, carryforwards available to offset future taxable income. Under the Tax Cuts and Jobs Act of 2017, or the Tax Act, federal NOLs generated after December 31, 2017 will be carried forward indefinitely with the yearly NOL utilization limited to 80% of taxable income. The Company has $324.7 million of such federal NOLs that do not expire. If not utilized, the federal carryforward losses generated prior to 2018 and the state carryforward losses will expire in various amounts beginning in 2031.

As of December 31, 2024, the Company had approximately $33.2 million of federal and $9.3 million of state credit carryforwards available to offset future taxable income. If not utilized, these credit carryforwards will expire in various amounts for federal purposes beginning in 2031. The state credits do not expire.

In assessing the realization of deferred tax assets, management considers whether it is more likely than not some portion or all of the deferred tax assets will not be realized. Management believes that, based on available evidence, both positive and negative, it is more likely than not that the deferred tax assets will not be utilized; therefore, a full valuation allowance has been recorded. The Company's valuation allowance increased by $50.0 million and $30.2 million for the years ended December 31, 2024 and 2023, respectively. The changes in the 2024 valuation allowance were primarily due to the addition of capitalized research and development costs, current year loss carryforwards and research and development credits. The changes in the 2023 valuation allowance were primarily due to the addition of capitalized research and development costs, current year loss carryforwards and research and development credits.

Utilization of the net operating loss carryforwards and credits may be subject to an annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended and similar state provisions. The annual limitations may result in the expiration of net operating losses and credits before utilization. The Company performed a Section 382 analysis through December 31, 2024. Federal net operating loss carryforwards of $367.6 million and state and local net operating loss carryforwards of $189.2 million are not expected to expire unutilized as a result of ownership changes identified through December 31, 2024. The Company has identified $0.1 million and $34.7 million of federal and state net operating losses, respectively, that will expire unused due to ownership changes,

and federal credits of $4.3 million that will not be able to be utilized due to ownership change limitation; these amounts have been excluded from the deferred tax assets table above. Further ownership changes subsequent to December 31, 2024 may be identified which could result in limitations to the amount of net operating losses and credits which may be utilized prior to expiration.

Uncertain Tax Benefits

The Company has the following activity relating to the gross amount of unrecognized tax benefits (in thousands):

	Year Ended December 31,	
	2024	2023
Beginning balance	$ 3,970	$ 2,726
Additions based on tax positions related to prior year	3,388	189
Reductions based on tax positions related to prior year	(1,726)	—
Additions based on tax positions related to current year	2,787	1,055
Ending balance	$ 8,419	$ 3,970

None of these uncertain tax positions will impact the Company's effective tax rate if assessed. The Company's policy is to classify interest and penalties associated with unrecognized tax benefits as income tax expense. The Company had no interest or penalty accruals associated with uncertain tax benefits in its consolidated balance sheet and consolidated statement of operations for the years ended December 31, 2024 and 2023. The Company files income tax returns in the United States, various states, and Australia. The Company is not currently under examination by any major tax jurisdictions nor has it been in the past. The tax years 2011 through 2024 remain effectively open for examination by the Internal Revenue Service and most state tax authorities because of net operating losses and credit carryovers.

Although it is reasonably possible that certain unrecognized tax benefits may increase or decrease within the next twelve months due to tax examination changes, settlement activities, expirations of statute of limitations, or the impact on recognition and measurement considerations related to the results of published tax cases or other similar activities, the Company does not anticipate any significant changes to unrecognized tax benefits over the next 12 months.

9. Net Loss Per Share

The Company calculates basic net loss per share by dividing net loss by the weighted-average number of shares of common stock outstanding. The weighted-average number of shares of common stock used in the basic and diluted net loss per share calculation include pre-funded warrants to purchase up to 38,543,577 and 40,492,923 shares of common stock for the years ended December 31, 2024 and 2023, respectively, as the pre-funded warrants are exercisable at any time for nominal cash consideration. The Company has generated a net loss in all periods presented, so the basic and diluted net loss per share are the same, as the inclusion of the potentially dilutive securities would be anti-dilutive.

The following outstanding potentially dilutive shares have been excluded from the calculation of diluted net loss per share due to their anti-dilutive effect:

	Year Ended December 31,	
	2024	2023
Stock options to purchase common stock	14,594,720	9,208,970
Shares subject to Employee Stock Purchase Plan	15,922	17,200
Unvested restricted stock units	770,028	495,579
Common warrants	8,104,615	8,427,508
Total	23,485,285	18,149,257

10. Segment Reporting

The Company has one reportable segment, which is related to the research and development of its product candidates focused on complement-mediated diseases of the body, brain and eye for which there is significant unmet medical need. The accounting policies of the one reportable segment are the same as those described in the summary of significant accounting policies. See Note 2—*Basis of Presentation and Significant Accounting Policies*.

The segment is managed on a consolidated basis and the CODM uses total operating expenses and consolidated net loss to assess performance, forecast future financial results and allocate resources. In assessing the Company's financial performance and making strategic decisions, the CODM regularly reviews operating expenses by function. This includes a review of budget versus actual expenses and direct program spend, which includes clinical costs, consultant fees, manufacturing expenses, and other direct external costs.

The following table presents the operations for the reportable segment during the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development - program expenses[1]	$ 79,548	$ 76,008
Research and development - personnel	24,291	23,893
General and administrative - personnel	6,578	6,896
Other general and administrative expenses[2]	22,073	16,595
Depreciation expense	2,150	2,148
Stock-based compensation	19,433	18,183
Total operating expense	154,073	143,723
Loss from operations	(154,073)	(143,723)
Interest and other income, net	15,873	9,486
Consolidated segment net loss	$ (138,200)	$ (134,237)

(1) Research and development - program expenses include other non-program specific expenses and other research expenses.
(2) Other general and administrative expenses include consulting and professional services fees for legal, accounting, tax, and facilities costs.

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

As of December 31, 2024, 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(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act). Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of the December 31, 2024, our disclosure controls and procedures are 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 specified in the SEC's 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 disclosures.

Management's Annual Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is 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.

Management has evaluated the effectiveness of our internal control over financial reporting as of December 31, 2024 using the criteria set forth in the 2013 *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2024.

This Annual Report on Form 10-K does not include an attestation report of the Company's independent registered public accounting firm regarding internal control over financial reporting. Pursuant to rules of the SEC, such attestation is not required for smaller reporting companies, which permit the Company to provide only management's report in this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2024 that materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitation on the Effectiveness of Internal Controls and Procedures

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls or our internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a 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 management override of the controls. The design of any system of controls is also based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of

changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Item 9B. Other Information.

Trading Arrangements of Section 16 Reporting Persons.

During the Company's last fiscal quarter, the Company's directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) adopted or terminated the contracts, instructions or written plans for the purchase or sale of the Company's securities set forth in the table below.

			Types of Trading Arrangement				
Name and Position	Action	Termination Date	Rule 10b5-1*	Non-Rule 10b5-1**	Total Shares of Common Stock to be Sold	Total Shares of Common Stock to be Purchased	Expiration Date
Douglas Love, Chief Executive Officer	Terminate	12/16/2024	X		37,994		1/22/2025

* Contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act.
** "Non-Rule 10b5-1 trading arrangement" as defined in Item 408(a) of Regulation S-K under the Exchange Act.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2025 Annual Meeting of Stockholders, or the Proxy Statement, which will be filed no later than 120 days after the end of our fiscal year ended December 31, 2024 and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our website at ir.annexonbio.com. The Code of Business Conduct and Ethics is intended to qualify as a "code of ethics" within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our directors or our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to a director one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

The remaining information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2025 Annual Meeting of Stockholders, or the Proxy Statement, which will be filed no later than 120 days after the end of our fiscal year ended December 31, 2024 and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item regarding executive compensation will be incorporated by reference to the information set forth in our Proxy Statement.

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

The information required by this item regarding security ownership of certain beneficial owners and management and our equity compensation plans will be incorporated by reference to the information set forth in our Proxy Statement.

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

The information required by this item regarding certain relationships and related transactions and director independence will be incorporated by reference to the information set forth in our Proxy Statement.

Item 14. Principal Accountant Fees and Services.

The information required by this item regarding principal accountant fees and services will be incorporated by reference to the information set forth in our Proxy Statement.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

1. Financial Statements

Information in response to this Item is included in Part II, Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

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

3. Exhibits

Exhibit Index

Exhibit No	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-39402	3.1	07/28/20	
3.2	Amended and Restated Bylaws.	8-K	001-39402	3.2	07/28/20	
4.1	Reference is made to Exhibits 3.1 through 3.2.					
4.2	Form of Common Stock Certificate.	S-1	333-239647	4.2	07/02/20	
4.3	Description of Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934.	10-K	001-39402	4.3	03/01/22	
4.4	Form of Pre-Funded Warrant.	8-K	001-39402	4.1	07/08/22	
4.5	Form of Common Warrant.	8-K	001-39402	4.2	07/08/22	
4.6	Form of Pre-Funded Warrant.	8-K/A	001-39402	4.1	12/22/23	
4.7	Form of Pre-Funded Warrant.	8-K	001-39402	4.1	06/07/24	
10.1	Amended and Restated Investors' Rights Agreement, dated June 30, 2020, by and among the Registrant and the investors listed therein.	S-1	333-239647	10.1	07/02/20	
10.2†	Exclusive (Equity) Agreement, dated November 21, 2011, by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University.	S-1	333-239647	10.2	07/02/20	
10.3	Lease, dated December 18, 2020, by and between the Registrant and HCP LS Brisbane, LLC.	8-K	001-39402	10.1	12/22/20	
10.4(a)+	2011 Incentive Award Plan.	S-1/A	333-239647	10.4(a)	07/20/20	
10.4(b)+	Form of Stock Option Agreement under 2011 Equity Incentive Plan.	S-1	333-239647	10.4(b)	07/02/20	

Exhibit No	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.5(a)+	2020 Incentive Award Plan.	S-8	333-240101	99.2(a)	07/24/20	
10.5(b)+	Form of Stock Option Grant Notice and Stock Option Agreement under the 2020 Incentive Award Plan.	S-1	333-239647	10.5(b)	07/02/20	
10.5(c)+	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2020 Incentive Award Plan.	S-1	333-239647	10.5(c)	07/02/20	
10.5(d)+	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2020 Incentive Award Plan.	S-1	333-239647	10.5(d)	07/02/20	
10.6+	Employee Stock Purchase Plan.	S-8	333-240101	99.3	07/24/20	
10.7+	Employment Agreement by and between the Registrant and Douglas Love, Esq.	S-1	333-239647	10.7	07/02/20	
10.8+	Employment Agreement by and between the Registrant and Jennifer Lew.	S-1	333-239647	10.9	07/02/20	
10.9+	Employment Agreement by and between the Registrant and Michael Overdorf.	S-1/A	333-239647	10.11	07/20/20	
10.10+	Non-Employee Director Compensation Program.					X
10.11+	Form of Indemnification and Advancement Agreement for directors and officers.	S-1	333-239647	10.12	07/02/20	
10.12+	Employment Agreement by and between the Registrant and Dean Richard Artis, Ph.D.	10-K	001-39402	10.12	03/06/22	
10.13	Sales Agreement, dated as of March 26, 2024, by and between Annexon Inc. and Cowen and Company, LLC.	S-3	333-278246	1.2	03/26/24	
10.14	Securities Purchase Agreement, dated July 7, 2022, by and among the Registrant and the Purchasers named within.	8-K	001-39402	10.1	07/08/22	
10.15+	Annexon, Inc. 2022 Employment Inducement Award Plan.	10-Q	001-39402	10.2(a)	08/08/22	
10.16+	Form of Stock Option Grant Notice and Stock Option Agreement under the 2022 Employment Inducement Award Plan.	10-Q	001-39402	10.2(b)	08/08/22	
10.17+	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2022 Employment Inducement Award Plan.	10-Q	001-39402	10.2(c)	08/08/22	
10.18+	Employment Agreement by and between the Registrant and Jamie Dananberg, M.D.	10-Q	001-39402	10.2#	08/07/23	

Exhibit No	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
19.1	Insider Trading Compliance Policy					X
21.1	List of subsidiaries.	S-1	333-239647	21.1	07/02/20	
23.1	Consent of Independent Registered Public Accounting Firm.					X
24.1	Power of Attorney (included in the signature page hereto).					X
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 amended.					X
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 amended.					X
32.1*	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 18 U.S.C. Section 1350, As Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, as amended.					X
97.1	Policy for Recovery of Erroneously Awarded Compensation.	10-K	001-39402	97.1	03/26/24	
101.INS	Inline XBRL Instance Document					X
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents					X
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)					X

+ Indicates management contract or compensatory plan.

† Certain portions of this document that constitute confidential information have been redacted in accordance with Regulation S-K, Item 601(b)(10).

* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, is not deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Annexon, Inc.

Date: March 3, 2025

By: /s/ Douglas Love, Esq.
Douglas Love, Esq.
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 3, 2025

By: /s/ Jennifer Lew
Jennifer Lew
Executive Vice President and 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 each of Douglas Love and Jennifer Lew his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, 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 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 to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitutes or 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/ Douglas Love, Esq. **Douglas Love, Esq.**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 3, 2025
/s/ Jennifer Lew **Jennifer Lew**	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 3, 2025
/s/ Thomas G. Wiggans **Thomas G. Wiggans**	Chairperson & Director	March 3, 2025
/s/ William H. Carson, M.D. **William H. Carson, M.D.**	Director	March 3, 2025
/s/ Jung E. Choi **Jung E. Choi**	Director	March 3, 2025
/s/ Bettina M. Cockroft, M.D. **Bettina M. Cockroft, M.D.**	Director	March 3, 2025
/s/ William Jones **William Jones**	Director	March 3, 2025
/s/ Muneer A. Satter **Muneer A. Satter**	Director	March 3, 2025
/s/ William D. Waddill **William D. Waddill**	Director	March 3, 2025