astria™

THERAPEUTICS

2024 ANNUAL REPORT

Dear Stockholders,

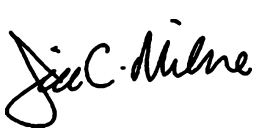
At Astria, our goal is to transform science that works into therapies that patients want. In the past year, we have made substantial progress, and believe we are in a strong position to become a leading allergy and immunology company. Our lead product candidate is navenibart, formerly called STAR-0215, a monoclonal antibody inhibitor of plasma kallikrein in Phase 3 clinical development for the treatment of hereditary angioedema (HAE). We believe navenibart could become the market-leading HAE therapy. We have also made significant progress this year on our second program, STAR-0310, a potential best-in-class monoclonal antibody OX40 antagonist that we are developing for the treatment of atopic dermatitis (AD) and potentially additional indications. We believe that we can significantly benefit patients' lives with these programs, and we are looking forward to advancing these programs in 2025.

We believe that navenibart has the potential to transform the way that people live with HAE and are thrilled with the enthusiasm for the program that we are seeing from patients and physicians. With the data that we have generated to-date, we believe that navenibart can provide rapid and sustained protection against HAE attacks, with administration only 2 or 4 times per year. In December 2024, we shared final results from the target enrollment patients in our Phase 1b/2 ALPHA-STAR clinical trial that supported this vision and enabled us to progress to our Phase 3 ALPHA-ORBIT clinical trial, which initiated early this year. The ALPHA-ORBIT trial is underway and enrolling patients, and we are executing with efficiency with the goal of bringing navenibart to patients as quickly as possible. Importantly, we are in a position to deliver on this key value proposition and expect that we have funding beyond Phase 3 topline data, which we expect in early 2027. We also anticipate initial safety and efficacy data for every 3-month and every 6-month administration from the ALPHA-SOLAR long-term open-label trial in mid-2025.

Over the course of 2024, we progressed STAR-0310 into Phase 1a development for the treatment of AD. STAR-0310 was designed to capitalize on the learnings of other OX40 receptor and OX40 ligand programs, with the goal of developing the best-overall OX40 therapy. The FDA granted clearance for the Investigational New Drug application for STAR-0310 in December 2024, and we initiated a Phase 1a trial in healthy subjects in January 2025. We anticipate initial results from the Phase 1a trial in the third quarter of 2025 to be informative on differentiation about the potential for STAR-0310. We believe STAR-0310 has the potential to address the need for a safe, effective and infrequently administered AD treatment.

We are grateful for your support and your belief in Astria's mission. In 2025, we are focused on effectively delivering on our programs, with the ultimate goal of bringing life-changing therapies to people living with allergic and immunologic diseases. We are in a strong position to execute on these goals, and we look forward to sharing updates on our exciting progress throughout the year.

Sincerely,
Jill C. Milne, Ph.D.
Chief Executive Officer
April 28, 2025



UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 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: 001-37467

Astria Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	**26-3687168** (IRS Employer Identification No.)
22 Boston Wharf Road **10th Floor** **Boston, Massachusetts** (Address of principal executive offices)	**02210** (Zip Code)

Registrant's telephone number, including area code **(617) 349-1971**

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

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

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or 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 ☒

Aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price for such stock on June 28, 2024: $370,232,653.

As of February 28, 2025, there were 56,434,219 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2025 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The registrant intends to file such proxy statement with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this Annual Report on Form 10-K relates.

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SIGNATURES

Summary of the Material Risks Associated with Our Business

Investing in our common stock involves a high degree of risk because our business is subject to numerous risks and uncertainties. The principal factors and uncertainties that make investing in our common stock risky include, among others:

- We are entirely dependent on the success of our product candidates, navenibart for the treatment of hereditary angioedema, or HAE, and STAR-0310 for the treatment of atopic dermatitis, or AD. We cannot give any assurance that we will generate preclinical, clinical or other data for navenibart or STAR-0310 sufficiently supportive to receive regulatory approval, which will be required before either can be commercialized.

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

- We will need substantial additional funding. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

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

- We have never obtained marketing approval for a product candidate, and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any future product candidate we may seek to develop.

- Clinical trials are costly, time consuming, difficult to enroll and inherently risky, and we may fail to demonstrate safety and efficacy on the timelines that we expect or to the satisfaction of applicable regulatory authorities. We also expect that any later stage clinical trials we conduct for STAR-0310 will be larger and more expensive when compared to those we are conducting, and plan to conduct, for navenibart because AD, the indication for which we are developing STAR-0310, is not a rare disease.

- Navenibart, STAR-0310 or any future product candidates may cause adverse events or undesirable side effects or have other unexpected properties that could delay or halt clinical trials, delay or prevent their regulatory approval, limit the commercial viability of an approved label, or result in significant negative consequences following marketing approval, if any.

- We face substantial competition from other pharmaceutical and biotechnology companies, and our operating results may suffer if we fail to compete effectively.

- Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results.

- We rely on in-licensed patent and other intellectual property rights for our STAR-0310 program and we may need to obtain licenses from third parties to other intellectual property rights for the development and commercialization of our STAR-0310 and navenibart programs; if we fail to comply with our existing or future obligations under these licenses, or if these licenses are terminated, we could lose license rights that are important to our business.

- We rely on third parties to conduct our preclinical studies and clinical trials. If they do not perform satisfactorily, our business could be significantly harmed.

- We will need to maintain a master cell bank for navenibart, a master cell bank for STAR-0310 and cell lines or banks for any other future biologic candidate that generate sufficient material for preclinical, nonclinical and clinical studies, and also build and maintain sufficient preclinical, clinical and commercial manufacturing drug substance, drug product and drug - device combination capacity, in each case, through third party manufacturers, for navenibart, STAR-0310 and any other future product candidate that advances into such stages, on the timetables and in a manner that, in each case, are consistent with our expected development timetables and financial projections, the failure of which could materially harm our business and operating results and require us to raise capital sooner than we expect.

- Our forecasts of cash usage and how long we expect our existing cash, cash equivalents and short-term investments to fund operating expenses and capital expenditure requirements may not be accurate and we may therefore use our cash, cash equivalents and short-term investments more rapidly than we expect, which could force us to delay, reduce or eliminate our product development programs or commercialization efforts, if any, and therefore materially harm our operating results, and we could be required to raise capital sooner than we expect.

- We have incurred significant losses since inception, have a limited operating history on which to assess our business, and anticipate that we will continue to incur significant losses for the foreseeable future.

- If we are unable to obtain and maintain sufficient patent and/or regulatory protection for product candidates, or if the scope of the patent and/or regulatory protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to commercialize such product candidates successfully may be adversely affected.

- The price of our common stock has been and is likely to continue to be highly volatile, which could result in substantial losses for our stockholders.

The summary risk factors described above should be read together with the text of the full risk factors below, in the section entitled “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K and the other information set forth in this Annual Report on Form 10-K, including under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial, may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance, strategy, future financial condition and clinical development programs. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, clinical development programs, regulatory filings and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include but are not limited to those described under the heading "*Summary of the Material Risks Associated with our Business*" and the "*Risk Factors*" in Part I, Item 1A of this Annual Report on Form 10-K and include, among other things, statements about:

- our expectations regarding the potential significance of the results from the Phase 1a clinical trial and ALPHA -STAR 1b/2 clinical trial of navenibart;
- our expectations regarding the timing of disclosure of initial safety and efficacy data from the ALPHA-SOLAR trial of navenibart;
- our expectations regarding the timing, nature, goals and results of the ALPHA-ORBIT Phase 3 clinical trial of navenibart, including the expected timing of release of topline results from such trial, and that favorable results from such trial and the ORBIT-EXPANSE long-term trial could support registration of navenibart as a potential treatment for hereditary angioedema, or HAE;
- our expectations regarding development and clinical testing of any drug device combination for dosing of navenibart;
- our expectations about the unmet medical need for HAE, the potential differentiating attributes of navenibart as a potential treatment for HAE, along with the potential market impact of such differentiation, the potential of navenibart to be a best-in-class, market-leading and patient-friendly treatment for HAE, and our vision for navenibart to become the first-choice preventative treatment for HAE with administration every three or six months with the goal of normalizing the lives of people living with HAE;
- the HAE treatment landscape, the product profile of existing HAE therapies and HAE therapies under development, and the estimated size and anticipated growth of the global HAE market;
- our expectations to continue to use third party contract manufacturers to meet our nonclinical, clinical and commercial needs for navenibart, STAR-0310, and any other development candidate and statements regarding having adequate clinical and commercial supply of navenibart, any drug device combination of navenibart and STAR-0310;
- the potential therapeutic benefits and potential attributes of STAR-0310 and our plans to develop STAR-0310 as a treatment for atopic dermatitis, or AD;
- our expectations about the anticipated timing of early proof-of-concept data from the Phase 1a clinical trial of STAR-0310;
- our expectations about the plans and potential design of a STAR-0310 proof-of-concept trial in AD patients;
- the potential commercial opportunity for STAR-0310 in AD and the likelihood that it can effectively compete in AD, assuming it is approved;
- the estimated size and anticipated growth of the AD market and the need for treatments for AD;

- the potential to pursue the development of STAR-0310 in additional indications;
- our goals and visions for the STAR-0310 program;
- our expectations regarding our ability to expand our pipeline;
- the potential benefits of any future acquisition, in-license, collaboration or preclinical development activities;
- our manufacturing plans, capabilities and strategy;
- our intellectual property position and strategy;
- our facilities plans and capacity;
- our management and mitigation of cybersecurity risks;
- our estimates regarding our cash runway, expenses, future revenue, capital requirements and needs for additional financing, including additional financing to fund our long-term operations;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "*Risk Factors*" in Part I, Item 1A of this Annual Report on Form 10-K, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward- looking statement, whether as a result of new information, future events or otherwise, except as required by law.

REFERENCES TO ASTRIA

Except as otherwise indicated herein or as the context otherwise requires, references in this Annual Report on Form 10-K to "Astria," "the Company," "we," "us," and "our" refer to Astria Therapeutics, Inc. and its consolidated subsidiaries.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for allergic and immunological diseases. Our focus is to develop first-choice therapies that improve the health and outcomes of patients with allergic and immunologic diseases. Our lead product candidate is navenibart, formerly known as STAR-0215, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in clinical development for the treatment of hereditary angioedema, or HAE, a rare, debilitating and potentially life-threatening disease. We believe that navenibart has the potential to be the market - leading and most patient-friendly chronic treatment option for HAE, based on proof-of-concept data in HAE patients and the existing HAE treatment landscape. Our second product candidate is STAR-0310, a monoclonal antibody OX40 antagonist that is in clinical development for the treatment of atopic dermatitis, or AD, an immune disorder associated with loss of skin barrier function and itching. We believe that with both of these programs, we are advancing a pipeline of products with meaningfully differentiated profiles based on validated mechanisms.

Navenibart

The treatment options for patients with HAE have improved in recent years, however, there is remaining unmet medical need and the global market for HAE therapy is strong and growing. The goal for navenibart is to develop a best-in-class monoclonal antibody inhibitor of plasma kallikrein able to provide long-acting, effective attack prevention for HAE. Our vision for navenibart is to lead the HAE market and become the first-choice preventative treatment for HAE with administration every three and six months with the goal of normalizing the lives of people living with HAE. Targeted plasma kallikrein inhibition can prevent HAE attacks by suppressing the pathway that generates bradykinin and causes excessive swelling. Navenibart is currently in clinical development and the U.S. Food and Drug Administration, or FDA, has granted Fast Track and Orphan Drug designations to navenibart for the treatment of HAE. The European Commission has granted Orphan Medicinal Product Designation to navenibart for the treatment of HAE.

In February 2025, we initiated a Phase 3 trial of navenibart called ALPHA-ORBIT. This global, randomized, double-blind, placebo-controlled trial is evaluating the efficacy and safety of navenibart over a 6-month treatment period in up to 135 adults and 10 adolescents (open-label), with Type 1 or Type 2 HAE. Adult patients will be randomized to receive one of three navenibart dose arms: 1) an initial 600 mg dose followed by 300 mg every 3 months (Q3M), 2) 600 mg every six months (Q6M), 3) 600 mg Q3M, or placebo; adolescents will receive an initial 600 mg dose followed by 300 mg Q3M. The dose arms support the potential to provide patient-centered dosing flexibility to people with HAE. The primary endpoint is time-normalized monthly HAE attacks at 6 months, and a key secondary endpoint includes the proportion of participants who are attack-free at 6 months. After 6 months, patients may be eligible to enter ORBIT-EXPANSE, a long-term trial, in which all patients will be treated with navenibart (open-label) and which will include a patient-centered flexible dosing period. The navenibart Phase 3 program will consist of the ALPHA-ORBIT Phase 3 trial and ORBIT-EXPANSE, which are designed to support registration globally. Top-line results from the ALPHA-ORBIT trial are anticipated in early 2027. In addition, to ease the administration of navenibart, we are developing both autoinjector and pre-filled syringe drug device combinations.

In February 2023, we initiated a Phase 1b/2 trial of navenibart called ALPHA-STAR, or Astria Long-acting Prophylaxis for Hereditary Angioedema: STAR-0215. This global, multi-center, open-label, single and multiple dose proof-of-concept clinical trial in people with HAE evaluated safety, tolerability, HAE attack rate reduction, pharmacokinetics, or PK, pharmacodynamics, or PD, and quality of life in patients three and six months after subcutaneous navenibart administration. We reported initial proof-of-concept data in HAE patients in March 2024. Target enrollment of 16 patients was achieved with all doses administered and we reported final results from ALPHA-STAR target enrollment in December 2024 which were as follows:

Cohort 1 evaluated a single 450 mg dose (n=4). The results for the cohort measured over 6 months were averages of:

- a 91% reduction in monthly attack rate;
- a 96% reduction in moderate and severe attacks; and
- a 94% reduction in acute rescue medication use; with
- 50% of patients being attack-free through 3 months of follow-up, and 25% being attack-free through 6 months of follow-up.

Cohort 2 evaluated a 600 mg dose followed by a 300 mg dose three months later, on Day 84 (n=6). The results for the cohort measured over 6 months were averages of:

- a 95% reduction in monthly attack rate;
- a 95% reduction in moderate and severe attacks; and
- a 94% reduction in acute rescue medication use; with
- 67% of patients being attack-free.

Cohort 3 received a 600 mg dose followed by a 600 mg dose one month later, on Day 28 (n=6). The results for the cohort measured over 6 months were averages of:

- a 92% reduction in monthly attack rate;
- a 96% reduction in moderate and severe attacks; and
- a 91% reduction in acute rescue medication use; with
- 67% of patients being attack-free.

Navenibart was generally well-tolerated with no serious treatment-emergent adverse events, or TEAEs, and no discontinuations. There were four non-severe and quickly resolved treatment-related TEAEs: one case of dizziness, one transient injection site reaction (rash), one case of injection site erythema, and one case of injection site pruritus. There were no injection site reactions of pain.

In October 2024, we presented new quality of life data from initial results from ALPHA-STAR at the American College of Allergy Asthma and Immunology (ACAAI) demonstrating that navenibart induced rapid improvements in quality of life in HAE patients. By day 28 after navenibart administration, 80% of participants achieved clinically meaningful improvements.

Enrollment in ALPHA-STAR was expanded and a total of 29 patients were enrolled in the trial in order to accelerate the collection of data to support potential regulatory filings and future approvals.

ALPHA-SOLAR, a long-term open-label trial assessing the long-term safety and efficacy of navenibart, is ongoing. All of the 29 patients from ALPHA-STAR have entered ALPHA-SOLAR. Participants are being assigned to receive navenibart in one of two dosing regimens: either 300mg Q3M or 600mg Q6M. We expect to report initial safety and efficacy data from ALPHA-SOLAR in mid-2025.

STAR-0310

We believe that OX40 inhibition has the potential to treat AD and other diseases. The current treatment options in AD are insufficient to address the needs of many patients, and standard of care treatments include steroids and topical medications which can treat symptoms but do not address the underlying disease. Our goal for STAR-0310 is to reduce disease activity, relapse rate, and treatment burden for patients with moderate-to-severe AD. STAR-0310 was engineered with YTE half-life extension technology to enable infrequent dosing. As a potential long-acting OX40 inhibitor, STAR-0310 aims to address the need for a safe, effective, and infrequently administered AD treatment.

In January 2025, we announced the initiation of our Phase 1a trial of STAR-0310 in healthy subjects. The Phase 1a randomized, double-blind, placebo-controlled single ascending dose trial is evaluating the safety, tolerability, PK, and immunogenicity of STAR-0310 in approximately 40 healthy adult participants. We anticipate early proof-of-concept results from the trial in the third quarter of 2025.

In May 2024, we shared preclinical results for STAR-0310 at the European Academy of Allergy and Clinical Immunology (EAACI) conference. STAR-0310 exhibited a long mean half-life of 26 days in cynomolgus monkeys compared to a half-life of 10-14 days for a typical non-half-life-extended IgG antibody. There was also an approximately 8-fold increase in binding affinity to human OX40 observed for STAR-0310 compared to telazorlimab, an earlier generation antibody prior to affinity maturation without half-life extension. Preclinical results demonstrated significantly less antibody-dependent cellular cytotoxicity, or ADCC, potential with STAR-0310 compared to rocatinlimab, an anti-OX40 monoclonal antibody in Phase 3 development by Amgen, Inc., with comparable potency. Having less ADCC in the context of robust potency could potentially result in a favorable safety profile and potentially wider therapeutic window for STAR-0310. We believe these preclinical results support the potential for STAR-0310 to have the best-in-class OX40 inhibitor profile.

Assuming positive results from the Phase 1a clinical trial, we are planning a proof-of-concept clinical trial of STAR-0310 in patients with AD. The goals of the proof-of-concept trial would be to demonstrate initial efficacy in AD as well as show differentiation in safety and tolerability and the potential for a reduced treatment burden as a result of extended half-life as compared to existing therapies.

Our Product Candidates

Navenibart

Navenibart is a monoclonal antibody that was designed to inhibit plasma kallikrein for the treatment of HAE. Plasma kallikrein is a critical component of the plasma contact system, which causes pathologic vascular permeability in Type I and Type II HAE. Navenibart is a humanized monoclonal antibody that was developed through a hybridoma screening and antibody optimization process. Following humanization and optimization for affinity and overall properties, the antibody was modified to increase its plasma half-life. This process resulted in navenibart, a humanized monoclonal antibody having the following desirable features: high affinity and kallikrein inhibitory activity, selectivity for plasma kallikrein compared to prekallikrein, reduced chemistry, manufacturing and controls or, CMC, liabilities and long plasma half-life. Based on these characteristics, preclinical experiments, clinical trial results with navenibart, and the HAE market landscape, we believe that navenibart has the potential to be a best-in-class and the most patient-friendly monoclonal antibody inhibitor of plasma kallikrein that could combine the benefits of infrequent dosing with the inhibition of attacks over long periods of time and low risk of injection pain while maintaining high levels of efficacy. We have established clinical proof of concept with our Phase 1b/2 ALPHA-STAR trial in people with HAE, and we believe that we can develop a differentiated, best-in-class new preventative therapy for HAE with a well-understood monoclonal antibody modality to provide patients with improved outcomes and quality of life.

Overview of HAE

HAE is a rare, autosomal dominant genetic disorder. The disease is characterized by recurrent, unpredictable, debilitating and potentially life-threatening edema in the skin, abdomen and airway. The vast majority of HAE cases (Type I and Type II) are caused by defects in the C1 esterase inhibitor gene. Deficiencies in the C1 esterase inhibitor gene result in overproduction of bradykinin, a key mediator of vasodilation and angioedema. In several other types of HAE, which are a small minority of cases, other mutations (e.g., in the Factor XII gene) can cause HAE. The estimated prevalence of Type I and Type II HAE range from 1 in 10,000 to 1 in 50,000 with fewer than 8,000 patients in the United States and 15,000 patients in Europe with HAE. There are active and knowledgeable HAE patient advocacy organizations in the United States and internationally.

Patients with HAE are typically diagnosed by the age of 20 with the average age of disease onset around 11. The severity and frequency of swelling attacks is highly variable even between family members.

The Role of Plasma Kallikrein in Hereditary Angioedema

Plasma kallikrein is an enzyme that cleaves high molecular weight kininogen, or HMWK, to release bradykinin. Normally, circulating C1 esterase inhibitor, or C1INH, limits the activation of plasma kallikrein from its precursor prekallikrein, and thereby prevents the release of excess bradykinin from the cleavage of HMWK by plasma kallikrein. In HAE associated with C1INH deficiency, plasma kallikrein is hyperactive, resulting in excessive bradykinin release. Bradykinin activates the bradykinin receptor, or B2R, in endothelial cells, resulting in increased vascular permeability and release of fluid into subcutaneous tissue spaces, or angioedema. Thus, unchecked plasma kallikrein activity is a critical component that causes pathologic vascular permeability and vasodilation in HAE, leading to excessive tissue swelling, a primary clinical symptom.

Unaddressed Market Opportunity

There are two treatment approaches to managing the unpredictable and recurrent edema attacks typically experienced by people with HAE. On-demand treatments are administered at the onset of an attack to reduce the severity and duration of the attack, and preventative treatments, which is the treatment approach that we are pursuing with navenibart, are taken chronically to reduce the frequency and severity of future attacks. The HAE treatment market is substantial and growing. We estimate that the HAE market was 2.8 billion dollars in 2023 and that it has potential to grow to 5.4 billion dollars by 2030. This growth is predicted based on patients being diagnosed earlier, more patients taking treatments to prevent HAE attacks, as well as expansion of available therapies in more geographic regions. In the United States, the FDA has approved four therapies for on-demand treatment of HAE: BERINERT® (C1 esterase inhibitor [human]), FIRAZYR® (icatibant injection), KALBITOR® (ecallantide) and RUCONEST® (C1 esterase inhibitor [recombinant]). For long-term preventative treatment of HAE, the FDA has approved the following four therapies: CINRYZE® (C1 esterase inhibitor [human]), HAEGARDA® (C1 esterase inhibitor subcutaneous [human]), TAKHZYRO® (lanadelumab-flyo) and ORLADEYO® (berotralstat).

With the exception of KALBITOR, these therapies are also approved and commercially available outside of the United States. The approved preventative therapies have provided HAE patients with treatment options but have limitations in dosing frequency, side effects and/or efficacy. CINRYZE and HAEGARDA are administered twice a week; CINRYZE by IV infusion and HAEGARDA by SC injection. TAKHZYRO is dosed every two weeks by SC injection. Dosing every four weeks may be considered in some patients. With these injectable therapies, patients have reported a desire for less burdensome administration. ORLADEYO is an oral capsule taken daily with food, and data from its approved label, while not comparative data, suggest a lower percentage reduction in attack rate than other available therapies. Historically, androgens and antifibrinolytic treatments have also been used as preventative treatment but they are associated with side effects such as hypertension, acne, hirsutism, rashes, amenorrhea, liver enzyme elevations and increased risk of thrombosis and their overall use has been declining with the availability of more-tolerable, HAE-specific therapies. Although there has been progress with recent innovation in therapies for HAE and, as described in the section entitled "Competition" in this Business section, there are a significant number of product candidates for HAE in clinical and preclinical development, we believe that there is remaining unmet medical need for potent and long duration of action preventative therapies to provide patients with lower burden of treatment and improved outcomes and quality of life. Market research with U.S. physicians and HAE patients has shown strong interest in a product with the potential profile of navenibart.

Clinical Trial Results and Development Plans

We initiated a Phase 1a clinical trial of navenibart in August 2022 and we announced initial results in December 2022. We presented additional preliminary results from the trial in February 2023 and further results were shared at the American College of Allergy, Asthma, and Immunology Conference in November 2023. Final results from the trial were shared at the American Academy of Allergy, Asthma, and Immunology Conference in February 2024. This Phase 1a randomized, double-blind, placebo-controlled single ascending dose clinical trial evaluated the safety, PK and PD of navenibart at a single U.S. center. Forty-one healthy subjects received a single dose of navenibart or placebo in four cohorts of 100mg, 300mg, 600mg, and 1200mg administered by SC injection or a fifth cohort of 600mg or placebo administered by IV injection. Navenibart was well-tolerated at all dose levels, with no serious adverse events or discontinuations due to an adverse event, and low risk of injection pain. Navenibart demonstrated rapid and sustained drug levels with dose-dependent PK. Navenibart achieved potentially therapeutic levels in less than one day after single doses greater than 100mg and showed an estimated half-life of up to 109 days. PK modeling of potential once-every-three-month and once-every-six-month clinical dose regimens over one to two years indicate navenibart has the potential for PK coverage that would confer HAE attack prevention. PD data showed statistically significant inhibition of Factor XIIa-induced plasma kallikrein activity compared to levels prior to dosing, observed using two different assay formats. The percentage inhibition of plasma kallikrein observed was consistent with clinical activity for doses greater than 300mg. Treatment-emergent ADAs were observed in eleven subjects from completed cohorts, all first observed on or after 140 or more days after the single dose of navenibart. ADAs were determined not to affect the PK or PD of navenibart.

These results support navenibart's target profile as a long-acting plasma kallikrein inhibitor and supported advancing navenibart to our Phase 1b/2 ALPHA-STAR trial, which we initiated in February 2023. This global, multi-center, open-label, single and multiple dose proof-of-concept clinical trial in people with HAE evaluated safety, tolerability, HAE attack rate, PK, PD, and quality of life in patients. Efficacy was assessed at three and six months after last navenibart administration. The trial had three cohorts, which all began with an eight week run-in period to assess baseline attack rate. Cohort 1 received a 450mg single dose of navenibart, Cohort 2 received an initial 600mg dose followed by a 300mg dose on Day 84, to simulate a potential three-month dosing regimen with maintenance doses of 300mg every three months. Cohort 3 received an initial 600mg dose, followed by a second 600mg dose 28 days later, to simulate a potential six-month dosing regimen with maintenance doses of 600mg every six months. All doses were administered subcutaneously and all patients in the trial were followed for six months after the last dose administered. We reported initial proof-of-concept data in HAE patients in the March 2024, and final results from the target enrollment in December 2024, which showed rapid onset of robust and durable efficacy, favorable safety and tolerability, and PK and PD consistent with sustained plasma kallikrein inhibition for both Q3M and Q6M administration. Final results from the target enrollment included reduction in mean monthly attack rate of 90-95% and up to a 67% attack-free rate over 6 months.

Enrollment in ALPHA-STAR was expanded and a total of 29 patients were enrolled in the trial in order to accelerate the collection of data to support potential regulatory filings and future approvals.

ALPHA-SOLAR, a long-term open-label trial assessing the long-term safety and efficacy of navenibart, is ongoing. All of the 29 patients from ALPHA-STAR have entered ALPHA-SOLAR. Participants are being assigned to receive navenibart in one of two dosing regimens: either 300mg Q3M or 600mg Q6M. We expect to report initial safety and efficacy data from ALPHA-SOLAR in mid-2025.

In February 2025, we initiated a Phase 3 trial of navenibart called ALPHA-ORBIT. This global, randomized, double-blind, placebo-controlled trial is evaluating the efficacy and safety of navenibart over a 6-month treatment period in up to 135 adults and 10 adolescents (open-label), with Type 1 or Type 2 HAE. Adult patients will be randomized to receive one of three navenibart dose arms: 1) an initial 600 mg dose followed by 300 mg every 3 months (Q3M), 2) 600 mg every six months (Q6M), 3) 600 mg Q3M, or placebo; adolescents will receive an initial 600 mg dose followed by 300 mg Q3M. The dose arms support the potential to provide patient-centered dosing flexibility to people with HAE. The primary endpoint is time-normalized monthly HAE attacks at 6 months, and a key secondary endpoint includes the proportion of participants who are attack-free at 6 months. After 6 months, patients may be eligible to enter ORBIT-EXPANSE, a long-term trial, in which all patients will be treated with navenibart (open-label) and which will include a patient-centered flexible dosing period. The navenibart Phase 3 program will consist of the ALPHA-ORBIT Phase 3 trial and ORBIT-EXPANSE, which are designed to support registration globally. Top-line results from the ALPHA-ORBIT trial are anticipated in early 2027. In addition, to ease the administration of navenibart, we are developing both autoinjector and pre-filled syringe drug device combinations.

STAR-0310

STAR-0310 is a monoclonal antibody OX40 antagonist incorporating YTE half-life extension technology that we are developing as a potential best-in-class treatment for AD as well as potentially for other allergic and immunological diseases. STAR-0310 is currently in clinical development. We licensed the rights to STAR-0310 under a license agreement, or the Ichnos License Agreement, that we entered into with Ichnos Sciences SA and Ichnos Sciences Inc., or collectively Ichnos, in October 2023, pursuant to which Ichnos granted to us an exclusive (even as to Ichnos and its affiliates), worldwide, and sublicensable right and license to certain patent rights and related know-how, or collectively the Licensed Intellectual Property, to develop, manufacture, and commercialize Ichnos' proprietary OX40 portfolio, which includes STAR-0310. Ichnos has also agreed not to develop or commercialize any product that directly modulates the OX40 receptor.

Overview of Atopic Dermatitis

AD is an immune disorder associated with loss of skin barrier function and itching. AD is caused by diverse mechanisms, spanning the spectrum of T cell-driven pathology. Approximately 90% of patients develop the disease within the first 5 years of life. AD is estimated to affect approximately 5% of the adult population in the United States, approximately half of which cases are reported to be moderate or severe. AD is a chronic disease and current treatment options are insufficient to address the needs of many patients. Standard of care treatments include steroids and topical medications, which can treat symptoms but do not address the underlying disease.

Role of OX40 in Atopic Dermatitis

OX40 is a receptor expressed on activated T cells that can target multiple effector T cell pathways with the potential for broad impact on the inflammatory cascade. Th1, Th2, and Th17/22 signaling can all contribute to AD. OX40 is upstream of Th1, Th2, and Th17/22 signaling and inhibition of OX40 could reduce the activity of this broad group of Th cells that are known to contribute to the disease.

Our goal for STAR-0310 is to reduce disease activity, relapse rate, and treatment burden for patients with moderate and severe AD in order to help normalize their lives. STAR-0310 was engineered with YTE half-life extension technology to enable infrequent dosing. As a potential long-acting OX40 inhibitor, STAR-0310 aims to address the need for a safe, effective, and infrequently administered AD treatment. By targeting OX40, STAR-0310 is designed to address a wide range of T cells involved in the heterogenous AD pathology, providing the potential for better efficacy and a broader addressable patient population.

Preclinical results support the potential for STAR-0310 to have the best-in-class OX40 inhibitor profile. By design, there is significantly less ADCC with STAR-0310 compared to rocatinlimab, an afucosylated anti-OX40 monoclonal antibody currently in Phase 3 clinical development by Amgen, Inc. Reduced ADCC has the potential for a more favorable safety profile and potentially wider therapeutic window for STAR-0310, which we believe provides the potential to drive more efficacy. STAR-0310 exhibits a long mean half-life of 26 days in cynomolgus monkeys, compared to 10-14 days in a typical non-half-life extended IgG1 antibody, and has comparable potency to rocatinlimab.

Unaddressed Market Opportunity

While there are available treatment options in AD, there remains unmet need for a therapy that is safe and effective for a broad patient population, with a low treatment burden. Standard of care includes systemic steroids and topical medications, which can treat symptoms but do not address underlying disease. Moderate-to-severe patients who do not respond to topical prescription therapies typically turn to biologics as their next option, and, subsequently, to Janus kinase, or JAK, inhibitors. We estimate that the moderate-to-severe AD treatment market was approximately $7 billion in 2022 and that it has the potential to grow to $26 billion by 2030 likely due to an increase in drug-treatment rates, especially with availability of new therapies and growth in biologics-treated patients owing to dermatologists' increasing comfort with biologics.

Four biologics have been approved by the FDA for the treatment of AD: DUPIXENT® (dupilumab), ADBRY® (tralokinumab-ldrm), EBLGYSS (lebrikizumab) and NEMLUVIO (nemolizumab) all of which are administered subcutaneously every two or four weeks and work by targeting the Th2 inflammatory pathway (IL-4/13, IL-13, and IL-31). Due to the heterogenicity of AD, there are many patients using these approved biologics who do not respond to treatment or experience limited efficacy. In addition, the FDA has approved two oral JAK inhibitors for the treatment of AD: RINVOQ® (upadacitinib) and CIBINQOTM (abrocitinib), and in the European Union OLUMIANT (baricitinib), another JAK inhibitor, is also approved for the treatment of AD. While these JAK inhibitors tend to have better efficacy than the approved biologics, they require daily oral administration and there are significant safety concerns, including a boxed warning, associated with JAK inhibitors.

Inhibiting OX40 could target multiple effector T cell pathways, and therefore has the potential to reduce the activity of a broader group of Th cells that are known to contribute to AD and potentially induce higher rates of clinical responses in more patients than currently available biologics. Additionally, OX40 inhibition has the potential to be disease modifying. Although there has been progress with recent innovation in therapies for AD and, as described in the section entitled "Competition" in this Business section, there are a significant number of product candidates for AD in clinical development, we believe that there is remaining unmet medical need for therapies with efficacy across a broader range of AD patients and a longer duration of action to provide patients with a lower treatment burden and improved outcomes and quality of life.

Development Plans

We shared preclinical profile results in May 2024 and received IND clearance from the FDA for STAR-0310 for the treatment of AD in December 2024. We initiated a Phase 1a clinical trial of STAR-0310 in healthy subjects in January 2025 and expect early proof of concept results in the third quarter of 2025, including PK and PD data and early signals on safety and tolerability. Assuming positive results from the Phase 1a clinical trial, we are planning a proof-of-concept clinical trial of STAR-0310 in patients with AD.

We also see an opportunity to explore the potential of STAR-0310 in additional allergic and immunological indications.

Competition

The development and commercialization of new drug products is highly competitive. If we successfully develop and commercialize any of our product candidates, we and any future collaborators will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Many of the entities developing and marketing existing and potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and commercialization. Even if we are able to successfully develop and commercialize a product, our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than our product.

Navenibart

We are developing navenibart for the potential preventative treatment of HAE. The key competitive factors affecting the success of navenibart, if approved, are likely to be its efficacy, safety, dosing frequency, method of administration, convenience, price and the availability of coverage and reimbursement from government and other third-party payors. In particular, we believe that the competitive position of navenibart will depend in part on whether it is approved for dosing once every three months, once every six months, or both, and whether we are able to obtain commercial approval of dosing with an autoinjector and pre-filled syringe for ease of administration.

In the United States, the FDA has approved four therapies for on-demand treatment of HAE: BERINERT, FIRAZYR, KALBITOR and RUCONEST. For long-term preventative treatment of HAE, the FDA has also approved four therapies: CINRYZE, HAEGARDA, TAKHZYRO and ORLADEYO. There are four main manufacturers of therapies for HAE: CSL Behring (BERINERT and HAEGARDA), Takeda (FIRAZYR, KALBITOR, CINRYZE and TAKHZYRO), Pharming (RUCONEST) and BioCryst (ORLADEYO). With the exception of KALBITOR, these therapies are also approved and commercially available outside of the United States (HAEGARDA is marketed as BERINERT SC outside of the United States). Historically, androgens and antifibrinolytic treatments have also been used as preventative treatment for HAE, however their use is declining with the availability of more-tolerable, HAE-specific therapies.

On-demand and preventative HAE therapies target one of three primary mechanisms. BERINERT, HAEGARDA, RUCONEST and CINRYZE are C1 Esterase Inhibitors (CI-INH) replacement therapies. FIRAZYR is a B2-receptor, or B2R, antagonist, and KALBITOR, TAKHZYRO and ORLADEYO target plasma kallikrein. TAKHZYRO is a monoclonal antibody and ORLADEYO is a small molecule inhibitor.

On-demand therapies are taken as needed; BERINERT and RUCONEST are IV infusions approved for adult and pediatric patients, FIRAZYR is an SC injection, approved for adults 18 and older, and KALBITOR is a series of three SC injections, approved for patients 12 years and older. KALBITOR must be administered by a healthcare professional to monitor for the risk of anaphylactic reactions.

Preventative therapies are taken chronically. CINRYZE is an IV infusion and HAEGARDA is an SC injection; both are administered twice a week and are approved for adult and pediatric patients 6 years and older. TAKHZYRO is an SC injection generally administered every two weeks; however, dosing every four weeks may be considered in some patients. TAKHZYRO is approved for patients 2 years and older.

ORLADEYO is an oral capsule taken once daily with food for patients 12 years and older. Given that TAKHZYRO is an approved monoclonal antibody inhibitor of plasma kallikrein, if navenibart is approved, we expect that it will compete most directly with TAKHZYRO. TAKHZYRO is the current global market leader of HAE preventative treatments.

We are aware of additional programs in development for HAE, which are focused largely on preventative approaches. For example, CSL Behring's garadacimab, a factor XIIa-inhibitory monoclonal antibody, or FXIIa mAb, has completed Phase 3 development for preventative treatment and submitted regulatory applications for marketing approval in regions including the United States. Garadacimab is approved in the European Union, Australia and the United Kingdom under the brand name ANDEMBRY. Ionis Pharmaceuticals, Inc.'s donidalorsen, an antisense inhibitor of prekallikrein synthesis has also completed Phase 3 development for preventative treatment and has a PDUFA date set for August 21, 2025. Pharvaris is developing two oral treatments, deucrictibant IR (immediate release) and deucrictibant XR (extended release). Deucrictibant is a small molecule inhibitor of B2R. Deucrictibant IR is in Phase 3 development for on-demand treatment. Based on a proof-of-concept Phase 2 trial with deucrictibant IR for preventative treatment, Pharvaris has initiated a Phase 3 trial for deucrictibant XR for preventative treatment. KalVista Pharmaceuticals, Inc. has an oral small molecule plasma kallikrein inhibitor sebetralstat for on-demand treatment of HAE that has completed Phase 3 development and has a PDUFA date set for June 17, 2025 (the Phase 2 trial for KVD824 for preventative treatment was terminated). Intellia Therapeutics has initiated a Phase 3 trial for NTLA-2002, a CRISPR knockout of the prekallikrein gene KLKB1. ADARx Pharmaceuticals, Inc. is conducting a Phase 2a trial for ADX-324, a prekallikrein siRNA inhibitor. Argo Biopharmaceutical Co., Ltd. is in Phase 1 development for PKK/BW-20805, an siRNA inhibitor. Preclinical development programs for preventative treatment include KalVista's oral FXIIa inhibitor and Ractigen Therapeutics' C1-INH gene (SERPING1) RNA activating program (RAG-12).

STAR-0310

We are developing STAR-0310 for the treatment of moderate-to-severe AD. The key competitive factors affecting the success of STAR-0310, if approved, are likely to be its safety and tolerability, efficacy, frequency of dosing, method of administration, convenience, price, and the availability of coverage and reimbursement from government and other third-party payors. In the United States, the FDA has approved two oral JAK inhibitors for the treatment of AD: RINVOQ and CIBINQO, and in the European Union OLUMIANT is also approved for the treatment of AD. Additionally, the FDA has approved four biologics for the treatment of AD: DUPIXENT,ADBRY, EBGLYSS, and NEMLUVIO. Standard of care also includes systemic steroids and topical medications which can treat symptoms but do not address underlying disease. Moderate-to-severe patients who do not respond to topical prescription therapies typically turn to biologics as their next option, and, subsequently, to JAK inhibitors.

Both DUPIXENT and ADBRY are administered subcutaneously every two weeks, and work by targeting the Th2 inflammatory pathway (IL-4/13, and IL-13, respectively). EBGLYSS and NEMLUVIO are administered subcutaneously every two or four weeks, and work by targeting the Th2 inflammatory pathway (IL-13 and IL-31, respectively). RINVOQ and CIBINQO require daily oral administration and are only available to patients who do not sufficiently respond to systemic therapies including biologics. While these JAK inhibitors tend to have better efficacy than the approved biologics, there are significant safety concerns including a boxed warning associated with JAK inhibitors.

We are aware of additional programs in development for AD, which are focused largely on biologic approaches. There are other companies that have product candidates in early-stage development for moderate-to-severe AD, including Nektar Therapeutics (rezpegaldesleukin), Pfizer (PF-07275315 and PF-07264660), LEO Pharma (temtokibart, LEO 152020), Akesobio (AK120), Connect Biopharma (rademikibart), Biosion (bosakitug), Apogee Therapeutics (APG777), InnoCare Pharma (ICP-332), Kymera Therapeutics (KTK-474), GSK (GSK1070806), UCB (UCB9741 and UCB1381), Union Therapeutics (orismilast), J&J (JNJ-7528 and JNJ-5939), Celldex Therapeutics (barzolvolimab), Evommune (EVO301 and EVO756), Eli Lilly (ucenprubart), Sanofi (SAR444656) and Opsidio (OpSCF).

Additionally, a new class of biologics is in clinical development targeting OX40, the same target as for STAR-0310. Amlitelimab (Sanofi) is an anti-OX40 ligand (OX40L) antibody that has started a Phase 3 trial. Rocatinlimab (Amgen) is an afucosylated OX40 receptor (OX40R) antibody currently in Phase 3 trials in AD. IMG-007 (Inmagene) is an OX40 receptor (OX40R) antibody that has completed a proof-of-concept trial in AD. APG990 (Apogee) is an anti-OX40 ligand antibody currently in a Phase 1a trial in AD. ABCL575 (AbCellera) is an anti-OX40 ligand antibody that is in preclinical development.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business. This includes plans to pursue and maintain patent protection intended to cover the composition of matter of navenibart and STAR-0310, their methods of use, and other related technologies and inventions that are important to our business. In addition to seeking patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for commercially important technologies, inventions and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others.

Navenibart Program

As of December 31, 2024, we own five patent families directed to navenibart. The first patent family is directed to the composition of matter of our product candidate navenibart and its use in treating various plasma kallikrein associated disorders including HAE. This family includes applications filed in North America (such as Canada, the U.S., and Mexico), South America (such as Argentina and Brazil), Europe, Asia (such as China, Japan, and Korea), the Middle East (such as Israel, Saudi Arabia, United Arab Emirates, and Kuwait), and Australia. These applications, if granted, would expire in 2042, assuming all maintenance fees are paid. Depending upon the circumstances, additional patent term may be available in certain jurisdictions, *e.g.*, the U.S., Japan, and Europe, via patent term extensions or supplementary protection certificates, although only patents directed to navenibart may be extended.

In the second patent family, we own one International (PCT) patent application directed to methods of treating various plasma-kallikrein associated disorders, including HAE, with specific dosing regimens of navenibart. Any national or regional stage applications derived from this PCT application, if filed and granted, would expire in 2043, assuming all maintenance fees are paid and without taking a potential patent term extension into account.

In a third patent family, we own one International (PCT) patent application and one U.S. patent application directed to methods of treating hereditary angioedema with navenibart. Any national or regional stage applications derived from this PCT application, if filed and granted, would expire in 2044, assuming all maintenance fees are paid. If the U.S. application is granted, it would expire in 2043, assuming all maintenance fees are paid and without taking a potential patent term extension into account.

In the fourth patent family, we own one U.S. provisional patent application directed to pharmaceutical formulations of navenibart. Any non-provisional patent applications claiming priority to this provisional application, if filed and granted, would expire in 2045, assuming all maintenance fees are paid and without taking a potential patent term extension into account.

In a fifth patent family, we own one U.S. provisional patent application directed to methods of treating hereditary angioedema with navenibart. Any non-provisional patent applications claiming priority to this provisional application, if filed and granted, would expire in 2045, assuming all maintenance fees are paid and without taking a potential patent term extension into account.

Anti-OX40 Program

In our anti-OX40 program, we have in-licensed from and co-own with Ichnos one International (PCT) patent application directed to the composition of matter of our product candidate STAR-0310 and its use in treating AD and other disorders. Any national or regional stage applications derived from this PCT application, if filed and granted would expire in 2044, assuming all maintenance fees are paid. Depending upon the circumstances, additional patent term may be available in certain jurisdictions, *e.g.*, the U.S., Japan, and Europe, via patent term extensions, although only patents directed to STAR-0310 may be extended.

In addition, we have also in-licensed five patent families from Ichnos directed to telazorlimab and telazorlimab-containing formulations, and their use. In particular, we have in-licensed one patent family directed to the telazorlimab composition of matter and its use with patents granted in North America (such as Canada, the U.S., and Mexico), Europe (such as Germany, France, Italy, Spain, Switzerland, and the UK), Asia (such as China, Japan, and Korea), and Australia. These patents are expected to expire in 2032, assuming all maintenance fees are paid. In the remaining patent families, we have in-licensed three pending U.S. patent applications and three pending European patent applications directed to telazorlimab uses and formulations, which if granted will expire from 2039 to 2040.

The patent positions for biopharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that our navenibart and STAR-0310 product candidates will be protected or remain protectable by enforceable patents, even if issued. We cannot predict whether the patent applications we are currently pursuing will issue as granted patents in any particular jurisdiction or whether the claims of any granted patent will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries where we may elect to file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office, or USPTO, in granting a patent. A United States patent term may be shortened, if a patent is terminally disclaimed by its owner, over another patent.

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. Similar provisions are available in Europe, Japan, and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that an issued United States patent covering navenibart or STAR-0310 may be entitled to a patent term extension. If either of our navenibart or STAR-0310 product candidates receives FDA approval, we intend to apply for a patent term extension, if available, to extend the term of the patent that covers the approved product candidate. We also intend to seek patent term extensions in any jurisdictions where they are available. However, there is no guarantee that the applicable authorities, including the USPTO or FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we may rely on other forms of regulatory and legislative non-patent exclusivity protection that are typically triggered by marketing approval of a product. In the United States, these include orphan drug exclusivity, pediatric exclusivity, new chemical entity exclusivity and, for biologics such as navenibart and STAR-0310, reference product exclusivity. The European Union, which we refer to as the European Union or EU, and many other key markets outside the United States have comparable forms of such exclusivity. However, there is no guarantee that we will obtain any of these forms of exclusivity protection for navenibart, STAR-0310 or any future product candidate.

We also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing processes. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors, contract research organizations, contract manufacturing organizations and potential collaborators, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

Manufacturing and Supply

We do not own or operate manufacturing facilities. We currently rely on third-party manufacturers and suppliers to make, package, label and distribute navenibart and STAR-0310. We expect to continue to do so to meet our nonclinical, clinical and commercial needs for navenibart, STAR-0310, and any other development candidate. We are developing a drug device combination product for navenibart and will need to rely on third-party contract manufacturers to manufacture any drug device combination product for navenibart or any other product candidate. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities and have hired qualified individuals with significant development and manufacturing experience to oversee our relationships with our contract development and manufacturing partners. Our third-party manufacturers are required to manufacture navenibart, STAR-0310, any drug device combination product and any future product candidates under current good manufacturing practices, or cGMPs, and other applicable laws and regulations. We have also adopted good inventory management and warehousing practices to minimize supply chain risks related to the manufacture of navenibart and STAR-0310.

Human Capital

As of December 31, 2024, we had 78 full-time employees, 45 of whom were primarily engaged in research and development activities. A total of 16 of our full-time employees have Ph.D. degrees. None of our employees are represented by a labor union and we believe our relations with our employees are good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. Our cash compensation, which consists of base salary and annual bonuses based upon bonus targets, are market-based and are designed to attract, retain and motivate our employees. The principal purposes of our equity incentive plans are also to attract, retain and motivate employees, selected consultants and the members of our board of directors through the granting of stock-based compensation awards, which have solely consisted of stock options, and to align such awards with the interests of our stockholders. We provide a comprehensive benefits package to help employees manage health, well-being, finances, and life outside of work, including health insurance, dental and vision insurance, life insurance, short-term and long-term disability insurance, paid sick leave, a 401(k) plan, including a matching contribution, a health savings account program, and paid vacation time.

We take pride in our people and work to create an inclusive environment where diversity is seen as a benefit and our differences are appreciated. We consider our people to be one of our biggest assets and believe that our investment in them through development opportunities, engagement, and retention is critical to our success.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, post-approval monitoring and reporting, and import and export of drugs and biologics. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources. The regulatory requirements applicable to product development, approval and marketing are subject to change, and regulations and administrative guidance often are revised or reinterpreted by government agencies in ways that may have a significant impact on our business.

Review and Approval of Drugs and Biologics in the United States

In the United States, the FDA approves and regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Biological products, or biologics, are licensed for marketing under the Public Health Service Act, or PHSA, and subject to regulation under the FDCA and related regulations. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products is referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug or biological product in the United States must typically secure the following:

- completion of preclinical laboratory tests in compliance with the FDA's good laboratory practice, or GLP, regulations;
- design of a clinical protocol and submission to the FDA of an IND which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- submission to the FDA of a new drug application, or NDA, for a drug candidate product and a biologics license application, or BLA, for a biological product requesting marketing for one or more proposed indications;
- review of the request for approval by an FDA advisory committee, where appropriate or if applicable;
- completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements to assure the product's identity, strength, quality and purity;
- completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of application and program fees pursuant to the Prescription Drug User Fee Act, or PDUFA;
- FDA approval of the NDA or BLA authorizing marketing of the drug or biological product for particular indications in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before a sponsor begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured substance or active pharmaceutical ingredient and the formulated product, as well as in vitro and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. These studies are typically referred to as IND-enabling studies. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

With passage of the FDA's Modernization Act 2.0 in December 2022, Congress eliminated provisions in both the FDCA and the PHSA that required animal testing in support of an NDA or BLA. While animal testing may still be conducted, the FDA was authorized to rely on alternative non-clinical tests, including cell-based assays, microphysiological systems, or bioprinted or computer models.

The IND and IRB Processes

An IND is a request for FDA authorization to administer an investigational product candidate to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biologic that is not the subject of an approved NDA or BLA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or CMCs. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical trial or to suspend an ongoing trial. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, a trial may only resume after the FDA has notified the sponsor that the trial may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the trial can proceed.

The FDA's primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board committee. This group provides authorization for whether a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk.

Once an IND application takes effect, the sponsor of the IND may amend the application as needed to ensure that the clinical trials are conducted according to protocols included in the IND. The FDA has indicated that sponsors are expected to submit amendments for new protocols or changes to existing protocols before implementation of the respective changes. New studies may begin, however, when the sponsor has submitted the change to the FDA for its review and the new protocol or changes to the existing protocol have been approved by the IRB with the responsibility for review and approval of the studies.

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

Additionally, some trials are overseen by a Data Monitoring Committee, an independent group of qualified experts organized by the trial sponsor. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory

alternative treatment options. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient INDs for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol.

When considering an IND for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical trials that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, sponsors are required to make policies for evaluating and responding to requests for expanded access for patients publicly available upon the earlier of initiation of a Phase 2 or Phase 3 clinical trial, or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In May 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Studies in Support of an NDA or BLA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written trial protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. The clinical investigation of an investigational drug or biological product is generally divided into four phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The four phases of an investigation are as follows:

- ***Phase 1.*** Phase 1 studies include the initial introduction of an investigational new drug or biological product into humans. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational drug or biological product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- ***Phase 2.*** Phase 2 includes the controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the investigational drug or biological product for a particular indication(s) in patients with the disease or condition under trial, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug or biological product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population.
- ***Phase 3.*** Phase 3 clinical trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug or biological product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug or biological product, and to provide an adequate basis for product approval.
- ***Phase 4.*** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily

indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans, or DAPs. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance was adopted from the International Council for Harmonisation's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

Clinical Studies Outside the United States in Support of FDA Approval

Sponsors frequently conduct clinical trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of U.S. approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Reporting Clinical Trial Results

Under the PHSA, sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or the NIH. In particular, information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases

for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017.

The PHSA grants the Secretary of Health and Human Services the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. As of December 19, 2024, the FDA has issued six notices of non-compliance, thereby signaling the government's willingness to begin enforcing these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Interactions with the FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. A development safety update report detailing the results of clinical trials must be submitted annually within 60 days of the anniversary dates that the IND went into effect. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product candidate; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Sponsors are also given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, there are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA meetings as well as end of phase meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product candidate, including, for example, meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues (should be limited to no more than two focused topics) and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

At the conclusion of these meetings, the FDA will typically provide its responses to questions posed by the sponsor regarding the clinical development program. The FDA will not indicate whether an NDA or BLA will be approved, but it will provide guidance to the sponsor on various questions, including whether an application should be submitted in the first place on the basis of the studies and data proposed by the sponsor. The agency may also generally express support for the sponsor's approach in the clinical development program but indicate that questions concerning whether the data support approval will be subject to review by the agency following its acceptance for filing of the NDA or BLA.

The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Manufacturing and Other Regulatory Requirements

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

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, an application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Generally, a sponsor must submit an initial pediatric study plan before the date on which the sponsor submits the required data and no later than either 60 days after the date of the end-of-phase 2 meeting or such other time as agreed upon between FDA and the sponsor. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Pursuant to the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, the FDA must send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. FDASIA further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response.

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued draft guidance that further describes the pediatric study requirements under PREA.

Submission and Review of an NDA or BLA by the FDA

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the proposed drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application must include all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's CMCs 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 a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product and the safety, purity and potency of the biological product to the satisfaction of the FDA.

The application is the vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new product candidate must be the subject of an approved NDA or BLA before it may be commercialized in the United States. Under PDUFA, the submission and review of most applications is subject to an application user fee, which may be substantial (for example, for federal fiscal year 2025 the application fee is approximately $4.3 million), and the sponsor of an approved application is also subject to an annual program fee, which for federal fiscal year 2025 is $403,889 per eligible prescription product. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses. If an application is withdrawn prior to the FDA acceptance for filing, 75% of these fees may be refunded to the sponsor. If an application is withdrawn after filing, a lower portion of these fees may be refunded in certain circumstances.

Following submission of an NDA or BLA, the FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. The review process and PDUFA goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

The FDA seeks to meet these timelines for review of an application but its ability to do so may be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. For example, during the past decade, the U.S. government has shut down several times and certain regulatory agencies, including the FDA, have had to furlough critical employees and stop critical activities, including the review of both NDAs and BLAs.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA or BLA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of

that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. With passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

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

The FDA's Decision on an NDA or BLA

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof." The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical trials to establish effectiveness of a new product. Under certain circumstances, however, FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. The FDA issued draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical trial to demonstrate effectiveness, but has not yet finalized that guidance.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review. Rather, for those seeking to challenge the FDA's CRL decision, the FDA has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after

commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

In the event that a sponsor wishes to make a change to a product that has been approved under an NDA or BLA, the sponsor must submit a supplemental application to the FDA. Such changes may include a revision of the labeling for the approved product, the addition of a new indication, a change in the dosage, strength or formulation of the product, or a modification of the manner in which the drug is manufactured. Under the timelines established pursuant to PDUFA, the standard review time for an NDA is generally 10 months from receipt of the application by the FDA.

Expedited Review Programs

The FDA is authorized to expedite the development of candidate products and review of applications in several ways. None of these expedited programs changes the standards for approval but each may help expedite the development or approval process governing product candidates.

- *Fast Track designation*. The sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

- *Breakthrough therapy designation.* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- *Regenerative advanced therapy.* With passage of the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an

effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, an additional post-approval confirmatory study(ies) to verify and describe the drug's clinical benefit or, in certain cases where the clinical endpoint takes longer to mature, the completion of the study. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

In December 2022, Congress modified certain provisions governing accelerated approval of drug and biological products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval trial of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics.

Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

Rare Pediatric Disease Priority Review Vouchers

With enactment of the FDASIA, Congress authorized the FDA under Section 529 of the FDCA to award priority review vouchers, or PRVs, to sponsors of certain rare pediatric disease product applications. This provision, which was further amended by the Advancing Hope Act of 2016, is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases.

Under this program, a sponsor who receives approval for a new drug or biologic for a rare pediatric disease may qualify for a PRV, which can be redeemed for priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product that receives a PRV may transfer, including by sale, the PRV to another sponsor and that PRV may be further transferred any number of times before it is used. A PRV entitles the holder to designate a single human drug application submitted under Section 505(b)(1) of the FDCA or Section 351 of the PHSA as qualifying for a priority review. An FDA priority review may expedite the review process of a marketing application reducing the review time from ten months after formal acceptance of the file to six months after formal acceptance of the file.

Specifically, in order for a sponsor to receive a PRV in connection with approval of a BLA or NDA, the investigational product must be designated by the FDA as a product for a rare pediatric disease prior to submission of the marketing application. A rare pediatric disease is a disease that is serious or life-threatening and which primarily affects individuals aged from birth to 18 years and fewer than 200,000 people in the United States. Alternatively, the disease may affect more than 200,000 people in the United States if there is no reasonable expectation that the cost of developing and making available in the United States a product for such disease or condition will be recovered from sales in the United States of such product. In addition, to qualify for a PRV, the sponsor must request the voucher and the BLA or NDA must itself be given priority review, rely on clinical data derived from studies examining a pediatric population and dosages of the product intended for that population, not seek approval for a different adult indication in the original rare pediatric disease product application and be for a product that does not include a previously approved active ingredient.

The Rare Pediatric Disease PRV program was originally set to expire in October 2020 but was extended for an additional six years with passage of the Coronavirus Response and Relief Supplemental Consolidated Appropriations Act of 2021. Under those statutory sunset provisions and subsequent legislation, the FDA was authorized to award a rare pediatric disease PRV if a sponsor had a rare pediatric disease designation for the drug or biologic before December 20, 2024, and the NDA or BLA for the candidate product is approved before September 30, 2026.

The rare pediatric disease PRV program was not reauthorized in 2024. Accordingly, unless and until the program is reauthorized by Congress, the FDA is no longer authorized to issue a rare pediatric disease designation for a drug or biologic. Further, if the program is not further extended by Congressional action and the deadlines for approval of an NDA or BLA are not extended, a sponsor that obtains approval of an NDA or BLA for a product designated for a rare pediatric disease will not receive a PRV if the application is approved after September 30, 2026.

Post-Approval Regulation

Drugs and 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 recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with 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 user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including 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 trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, or HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval.

In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws. The Prescription Drug Marketing Act, or the PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act became effective in the U.S., mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and effectiveness of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and effectiveness for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor.

Generic Drugs and Regulatory Exclusivity

In 1984, with passage of the Hatch-Waxman Act, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA until any applicable period of regulatory exclusivity for the RLD has expired. The FDCA provides a period of five years of regulatory exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of regulatory exclusivity if the NDA includes reports of one or more new clinical trials, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

Biosimilars and Regulatory Exclusivity

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, was enacted in the United States and included the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, the FDA has approved a number of biosimilars and it has also issued numerous guidance documents outlining its approach to reviewing and licensing biosimilars and interchangeable biosimilars under the PHSA.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for

products administered multiple times) that the biologic and the reference biologic may be 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 of first licensure of the reference product. The FDA may not approve a biosimilar product 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 develop and receive approval of a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. In December 2022, Congress clarified through FDORA that the FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference product and the exclusivity period may be shared amongst multiple first interchangeable products. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biological product intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA or BLA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if the company with orphan drug exclusivity is not able to meet market demand or the subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. Orphan drug exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. Orphan drug exclusivity also could block the approval of one of our product candidates for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication for which we are seeking approval, or if our product candidate is determined to be contained within the scope of the competitor's product for the same indication or disease. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Pediatric Exclusivity

Pediatric exclusivity is another type of regulatory exclusivity in the United States and, if granted, provides for the attachment of an additional six months of regulatory exclusivity, including orphan drug exclusivity. For drug products, the six month regulatory exclusivity may be attached to the term of any existing patent or regulatory exclusivity available under the Hatch-Waxman Act provisions of the FDCA. For biologic products, the six month period may be attached to any existing regulatory exclusivities but not to any patent terms. This six-month exclusivity may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study, provided that at the time pediatric exclusivity is granted there is not less than nine

months of term remaining. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

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

Review and Clearance or Approval of Medical Devices in the United States

Medical devices in the United States are strictly regulated by the FDA. Under the FDCA, a medical device is defined as an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component part, or accessory which is, among other things: intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. This definition provides a clear distinction between a medical device and other FDA regulated products such as drugs. If the primary intended use of the product is achieved through chemical action or by being metabolized by the body, the product is usually a drug. If not, it is generally a medical device.

Unless an exemption applies, a new medical device may not be marketed in the United States until it has been cleared through filing of a 510(k) premarket notification, or 510(k), or approved by the FDA pursuant to a premarket approval application, or PMA. The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably ensure their safety and effectiveness. Class I devices have the lowest level or risk associated with them, and are subject to general controls, including labeling, premarket notification and adherence to the Quality System Regulation. Class II devices are subject to general controls and special controls, including performance standards. Class III devices, which have the highest level of risk associated with them, such as life sustaining, life supporting or some implantable devices, or devices that have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally marketed device, are subject to most of the aforementioned requirements as well as to premarket approval.

A 510(k) must demonstrate that the proposed device is substantially equivalent to another legally marketed device, or predicate device, that did not require premarket approval. In evaluating a 510(k), the FDA will determine whether the device has the same intended use as the predicate device, and (a) has the same technological characteristics as the predicate device, or (b) has different technological characteristics, and (i) the data supporting substantial equivalence contains information, including appropriate clinical or scientific data, if deemed necessary by the FDA, that demonstrates that the device is as safe and as effective as a legally marketed device, and (ii) does not raise different questions of safety and effectiveness than the predicate device. Most 510(k)s do not require clinical data for clearance, but the FDA may request such data. The FDA seeks to review and act on a 510(k) within 90 days of submission, but it may take longer if the agency finds that it requires more information to review the 510(k). If the FDA concludes that a new device is not substantially equivalent to a predicate device, the new device will be classified in Class III and the manufacturer will be required to submit a PMA to market the product. PMA applications are subject to an application fee. For federal fiscal year 2025, the standard fee is $540,783 and the small business fee is $135,196.

Modifications to a 510(k)-cleared medical device may require the submission of another 510(k) or a PMA if the changes could significantly affect safety or effectiveness or constitute a major change in the intended use of the device. Modifications to a 510(k)-cleared device frequently require the submission of a traditional 510(k), but modifications meeting certain conditions may be candidates for FDA review under a Special 510(k). If a device modification requires the submission of a 510(k), but the modification does not affect the intended use of the device or alter the fundamental technology of the device, then summary information that results from the

design control process associated with the cleared device can serve as the basis for clearing the application. A Special 510(k) allows a manufacturer to declare conformance to design controls without providing new data. When the modification involves a change in material, the nature of the "new" material will determine whether a traditional or Special 510(k) is necessary.

A clinical trial is typically required for a PMA application, and in a small percentage of cases, the FDA may require a clinical study in support of a 510(k) submission. A manufacturer that wishes to conduct a clinical study involving the device is subject to the FDA's IDE regulation. The IDE regulation distinguishes between significant and non-significant risk device studies and the procedures for obtaining approval to begin the study differ accordingly. Also, some types of studies are exempt from the IDE regulations. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices are devices that are substantially important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health. Studies of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical study. Non-significant risk devices are devices that do not pose a significant risk to the human subjects. A non-significant risk device study requires only IRB approval prior to initiation of a clinical study.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the Quality System Regulation, which covers the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging, and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Review and Approval of Combination Products in the United States

Under the FDA's regulations, a combination product is defined as: (a) a product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product. This term may include a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity (a "single-entity" combination product); two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products ("co-packaged" combination product); a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product (a "cross-labeled" combination product); or any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect (a "cross-labeled" investigational combination product).

The FDA has established an Office of Combination Products to serve as a focal point for combination product issues and for medical product classification and assignment issues for agency staff and industry. That office issues guidance and regulations to clarify the regulation of combination products and is responsible for assigning products to an FDA center for premarket review and regulation where their classification or assignment is unclear or in dispute. Combination products are assigned to an FDA center based on a determination of the "primary mode of action" or PMOA of the combination product. The FDCA defines PMOA as "the single mode of action of a combination product that provides the most important therapeutic action of the combination product." For example, if the PMOA of a device-biological combination product is attributable to the biological product, the FDA Division responsible for premarket review of that biological product would have primary jurisdiction for the combination product. One investigational application is generally sufficient for a combination product, but that application must include all information on the entire combination product. In most cases, the type of investigational application is that typically required by the lead center. Thus, if the drug constituent part of a drug/device combination product provides the PMOA, the investigation would be under an IND.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities, including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes

and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. While we are not a covered entity, as a business associate, we could be subject to penalties, including criminal penalties, and contractual damages if we knowingly obtain or further disclose PHI from a covered entity, such as a health care provider or clinical research site, and therefore we must ensure the proper authorizations are in place before we, or our vendors or business partners, obtain access to any PHI.

In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

The California Consumer Privacy Act, or CCPA, imposes many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the European Union's General Data Protection Regulation, or GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. Additionally, starting on January 1, 2023, the California Privacy Rights Act, or CPRA, significantly modified the CCPA, including by expanding consumers' rights, particularly with respect to certain sensitive personal information, and creating new principles, such as data minimization, purpose limitation and storage limitation. The CPRA also created a new state agency with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how they are interpreted and exemplify the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities.

In addition to California, at least eighteen other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2024. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act.

Review and Approval of Medical Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods.

Non-clinical Studies

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with GLP principles as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trial Approval in the European Union

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one European Union Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the European Medicines Agency, or the EMA, and available to clinical trial sponsors, competent authorities of the European Union Member States and the public.

Beyond streamlining the process, the new regulation includes a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors, and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all European Union Member States in which an application for authorization of a clinical trial has been submitted, which we refer to as the Member States concerned. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Member State concerned. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the European Union Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different European Union Member States, the competent authorities in each of these European Union Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

The Clinical Trials Regulation foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the Clinical Trials Regulation varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the Clinical Trials Regulation.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated agency contact and rapporteur from the Committee for Medicinal Products for Human Use, or CHMP, or Committee for Advanced Therapies are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level.

Pediatric Studies

In the European Economic Area, or EEA, companies developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA's pediatric committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date.

Marketing Authorization

In the EEA, medicinal products can only be commercialized after obtaining a marketing authorization. Marketing authorizations, or MAs, for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union Member States. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure, the maximum timeframe for the evaluation of a marketing authorization application is 210 days, excluding clock stops, when additional written or oral information is to be provided by the sponsor in response to questions asked by the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a "major public health interest." Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other concerned European Union Member States of an assessment of an application for marketing authorization conducted by one European Union Member State, known as the reference European Union Member State. In accordance with this procedure, a sponsor submits an application for marketing authorization to the reference European Union Member State and the concerned European Union Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference European Union Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned European Union Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned European Union Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all European Union Member States.

Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate preclinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the sponsor shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a single marketing authorization for the medicinal product is in the interest of patients in the EU.

Conditional Marketing Authorization

In particular circumstances, E.U. legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5) and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive; and (5) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data.

A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new clinical studies and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization, but applicants can also request EMA to conduct an accelerated assessment, for instance in cases of unmet medical needs.

Exceptional Circumstances

A MA may also be granted "under exceptional circumstances" under Article 14(8) of Regulation (EC) No 726/2004 when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable. Under these procedures, before granting the MA, the EMA or the competent authorities of the European Union Member States make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Periods of Authorization and Renewals

Marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file with respect to quality, safety and effectiveness, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization, or if initially placed on the market, is no longer actually present on the market for three consecutive years, ceases to be valid (the so-called sunset clause).

Regulatory Requirements After Marketing Authorization

Following marketing authorization of a medicinal product in the European Union, the holder of the authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the European Union's stringent pharmacovigilance or safety reporting, as well as rules potentially requiring post-authorization studies and additional monitoring obligations. In addition, the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with applicable European Union

laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice.

These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union. Finally, the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83EC, as amended, and European Union Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the European Union.

Regulatory Data Protection

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity prevents sponsors for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company can complete a full MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

In this context, it should be noted that the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products was published in April 2023 and includes, among other things, provisions that would potentially reduce the duration of regulatory data protection. The European Parliament requested several amendments in April 2024. At this time, the proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry in the long term, if and when adopted.

Pediatric Exclusivity

Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate, or SPC (if any is in effect at the time of approval), even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and, without incentives, it is unlikely that that the marketing of the product in the European Union would generate sufficient return to justify the necessary investment in its development. In addition to either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the sponsor's medicinal product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all European Union Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for trial

protocols, European Union-wide authorization through the centralized marketing authorization procedure and a reduction or elimination of registration and marketing authorization fees. During the period of market exclusivity, a marketing authorization may not be granted in the European Union for a "similar medicinal product" to the authorized orphan product for the same indication, except in the following limited circumstances: (i) the marketing authorization holder for the original orphan medicinal product consents to the authorization of the second orphan medicinal product; (ii) the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities of the product; or (iii) it is established that the second product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The period of market exclusivity may be reduced to six years if, at the end of the fifth year, it can be demonstrated on the basis of available evidence that the original orphan medicinal product no longer meets the criteria for orphan designation, including if it is sufficiently profitable not to justify maintenance of market exclusivity.

Patent Term Extensions

The EU also provides for patent term extension through SPCs. The rules and requirements for obtaining an SPC are set out in Regulation (EC) 469/2009 and are similar to those in the U.S. An SPC may extend a patent right for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained. Although SPCs are available throughout the EU, sponsors must apply on a country-by-country basis, and SPCs are valid on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the EU.

Review and Approval of Medical Devices in the European Union

The EU has adopted numerous directives and standards regulating, among other things, the design, manufacture, clinical trials, labeling, approval and adverse event reporting for medical devices. In the European Union, or the European Union, medical devices must comply with the Essential Requirements in Annex I to the currently applicable European Union Medical Devices Directive (Council Directive 93/42/EEC), or the Essential Requirements. Compliance with these requirements is a prerequisite to be able to affix the CE Mark of Conformity to medical devices, without which they cannot be marketed or sold in the EEA.

To demonstrate compliance with the Essential Requirements a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. Except for low risk medical devices, where the manufacturer can issue a CE Declaration of Conformity based on a self-assessment of the conformity of its products with the Essential Requirements, a conformity assessment procedure requires the intervention of a third-party organization designated by competent authorities of a European Union country to conduct conformity assessments, or a Notified Body. Notified Bodies are independent testing houses, laboratories, or product certifiers typically based within the European Union and authorized by the European member states to perform the required conformity assessment tasks, such as quality system audits and device compliance testing. The Notified Body would typically audit and examine the product's Technical File and the quality system for the manufacture, design and final inspection of the product before issuing a CE Certificate of Conformity demonstrating compliance with the relevant Essential Requirements.

Medical device manufacturers must carry out a clinical evaluation of their medical devices to demonstrate conformity with the relevant Essential Requirements. This clinical evaluation is part of the product's Technical File. A clinical evaluation includes an assessment of whether a medical device's performance is in accordance with its intended use, and that the known and foreseeable risks linked to the use of the device under normal conditions are minimized and acceptable when weighed against the benefits of its intended purpose. The clinical evaluation conducted by the manufacturer must also address any clinical claims, the adequacy of the device labeling and information (particularly claims, contraindications, precautions and warnings) and the suitability of related Instructions for Use. This assessment must be based on clinical data, which can be obtained from clinical studies conducted on the devices being assessed, scientific literature from similar devices whose equivalence with the assessed device can be demonstrated or both clinical studies and scientific literature.

With respect to implantable devices or devices classified as Class III in the European Union, the manufacturer must conduct clinical studies to obtain the required clinical data, unless relying on existing clinical data from similar devices can be justified. As part of the conformity assessment process, depending on the type of devices, the Notified Body will review the manufacturer's clinical evaluation process, assess the clinical evaluation data of a representative sample of the device's subcategory or generic group, or assess all the clinical evaluation data, verify the manufacturer's assessment of that data and assess the validity of the clinical evaluation report and the conclusions drawn by the manufacturer.

Even after a manufacturer receives a CE Certificate of Conformity enabling the CE mark to be placed on it products and the right to sell the products in the EEA countries, a Notified Body or a competent authority may require post-marketing studies of the products. Failure to comply with such requirements in a timely manner could result in the withdrawal of the CE Certificate of Conformity and the recall or withdrawal of the subject product from the European market.

A manufacturer must inform the Notified Body that carried out the conformity assessment of the medical devices of any planned substantial changes to the devices which could affect compliance with the Essential Requirements or the devices' intended purpose. The Notified Body will then assess the changes and verify whether they affect the product's conformity with the Essential Requirements or the conditions for the use of the devices. If the assessment is favorable, the Notified Body will issue a new CE Certificate of Conformity or an addendum to the existing CE Certificate of Conformity attesting compliance with the Essential Requirements. If it is not, the manufacturer may not be able to continue to market and sell the product in the EEA.

In the EU, medical devices may be promoted only for the intended purpose for which the devices have been CE marked. Failure to comply with this requirement could lead to the imposition of penalties by the competent authorities of the European Union Member States. The penalties could include warnings, orders to discontinue the promotion of the medical device, seizure of the promotional materials and fines. Promotional materials must also comply with various laws and codes of conduct developed by medical device industry bodies in the European Union governing promotional claims, comparative advertising, advertising of medical devices reimbursed by the national health insurance systems and advertising to the general public.

Additionally, all manufacturers placing medical devices in the market in the EU are legally bound to report any serious or potentially serious incidents involving devices they produce or sell to the competent authority in whose jurisdiction the incident occurred. In the European Union, manufacturers must comply with the European Union Medical Device Vigilance System. Under this system, incidents must be reported to the relevant authorities of the European Union countries, and manufacturers are required to take Field Safety Corrective Actions, or FSCAs, to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. An incident is defined as any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient or user or of other persons or to a serious deterioration in their state of health. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device. FSCAs must be communicated by the manufacturer or its European Authorized Representative to its customers and to the end users of the device through Field Safety Notices.

Review and Approval of Medical Products in the United Kingdom

The UK's withdrawal from the EU, commonly referred to as Brexit, took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, which entered into force on May 1, 2021. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol, as amended by the so - called Windsor Framework agreed in February 2023. As of January 1, 2025, the changes introduced by the Windsor Framework resulted in the MHRA being responsible for approving all medicinal products destined for the United Kingdom market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU.

As of January 1, 2024 on, a new international recognition procedure, or IRP, applies which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or an MRDC positive end of procedure outcome is an RR authorization for the purposes of IRP.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision in July 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved.

Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States.

In March 2010, President Obama signed the ACA into law. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act.

These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since the enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. In June 2021, the U.S. Supreme Court dismissed the most recent judicial action challenging the constitutionality of the ACA after finding that the plaintiffs do not have standing to bring the action. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of products from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted Section 804 Importation Program proposals to the FDA. On January 5, 2023, the FDA approved Florida's plan for Canadian product importation. That state now has authority to import certain products from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each product selected for importation, which must be approved by the FDA. The state will also need to relabel the products and perform quality testing of the products to meet FDA standards.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act of 2022, or the IRA, has been delayed by Congress to January 1, 2032.

More recently, on August 16, 2022, the IRA was signed into law by President Biden. The IRA has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the IRA subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the IRA by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The IRA also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The IRA also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year, and shifts some of the cost sharing for such costs to drug manufacturers.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, the HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. This second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

In June 2023, Merck & Co. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution.

Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal. Litigation involving these and other provisions of the IRA will continue with unpredictable and uncertain results.

In addition, at the federal level in the United States, in February 2023, CMS announced a model that would allow CMS to pay less for drugs and biologics approved through FDA's accelerated approval pathway before a clinical benefit has been confirmed by the required confirmatory studies. If implemented, this would impact the price that CMS would pay for Medicare Part B drugs and biologics that fit within CMS's criteria for lower payments.

At the state level, individual states are increasingly aggressive 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. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers and wholesale distributors, to disclose information about pricing of pharmaceuticals. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements.

Restrictions under applicable federal and state health care laws and regulations, include the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order

or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program, such as Medicare and Medicaid; the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; HIPAA, which imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program; the Foreign Corrupt Practices Act which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-United States officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the CMS, within the HHS, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Similar restrictions apply to the regulation of medical products in the EU and UK. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the EU's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the EU and are also subject to EU Member State laws. The failure to comply with these and other EU requirements can also lead to significant penalties and sanctions.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in foreign jurisdictions, including the EU and UK. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States and the UK Bribery Act 2010. Payments made to physicians in certain EU Member States must be publicly disclosed and often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. The failure of a company to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Our Corporate Information

Our executive offices are located at 22 Boston Wharf Road, 10th Floor, Boston, Massachusetts, 02210, and our telephone number is (617) 349-1971. Our website address is www.astriatx.com. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website located at www.astriatx.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission, or the SEC. These reports are also available at the SEC's Internet website at www.sec.gov. Our website and the information contained therein or connected thereto are not intended to be incorporated into this Annual Report on Form 10-K.

A copy of our Corporate Governance Guidelines, Code of Business Conduct and Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.astriatx.com, under "For Investors — Corporate Governance".

Item 1A. Risk Factors

We operate in a dynamic and rapidly changing business environment that involves risks and substantial uncertainty. The following discussion addresses risks and uncertainties that could cause, or contribute to causing, actual results to differ from expectations in material ways. In evaluating our business, investors should pay particular attention to the risks and uncertainties described below, some of which have manifested and any of which may occur in the future, and in other sections of this Annual Report on Form 10-K and in our subsequent filings with the U.S. Securities and Exchange Commission, or SEC. These risks and uncertainties, or other events that we do not currently anticipate or that we currently deem immaterial also may affect our results of operations, cash flows and financial condition. The trading price of our common stock could also decline due to any of these risks, and you could lose all or part of your investment.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Our business is entirely dependent on the success of navenibart as a potential treatment for HAE and STAR-0310 as a potential treatment for AD.

Our business is entirely dependent on the success of navenibart, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in clinical development for the potential treatment of hereditary angioedema, or HAE, and STAR-0310, a potential best-in-class monoclonal antibody OX40 antagonist that incorporates YTE half-life extension technology in clinical development for the potential treatment of atopic dermatitis, or AD. We presented results from a Phase 1a clinical trial of navenibart in healthy subjects in December 2022, February 2023, November 2023 and February 2024. We initiated the Phase 1b/2 ALPHA-STAR trial of navenibart in patients with HAE in February 2023. We reported initial proof-of-concept data in patients with HAE from the ALPHA-STAR trial in March 2024 and we reported positive final results from target enrollment in such trial in December 2024. We initiated a Phase 3 trial, known as ALPHA-ORBIT, for navenibart in February 2025, which together with our planned long-term trial, known as ORBIT-EXPANSE, are expected to provide data to potentially support marketing approval submissions with the FDA, EMA and regulators in other jurisdictions, assuming favorable data from such trials. We also submitted an investigational new drug application, or IND, for STAR-0310, which was cleared by the FDA in December 2024. We initiated a Phase 1a clinical trial of STAR-0310 in healthy subjects in January 2025 and we expect to report initial results from this trial in the third quarter of 2025, including PK data and early signals on safety and tolerability. Assuming positive results from the Phase 1a clinical trial, we are planning a proof-of-concept clinical trial of STAR-0310 in patients with AD. We cannot give any assurance that we will generate preclinical, clinical or other data for navenibart or STAR-0310 sufficiently supportive to receive marketing approval, which will be required before either can be commercialized. We may, among other things, experience difficulties with patient recruitment, enrollment and retention, quality and provision of materials and supplies necessary to manufacture sufficient quantities of drug product to meet our preclinical study and clinical trial needs on a timely basis, or safety signals or pharmacodynamic, pharmacokinetic or efficacy data that does not align with our target profile for navenibart or STAR-0310. Navenibart and STAR-0310 will require significant preclinical, clinical and nonclinical development, regulatory review and marketing approval, substantial investment, access to sufficient commercial manufacturing capacity, and significant marketing efforts before we can generate any revenue from product sales.

We are developing a drug device combination for administration of navenibart with an autoinjector and pre-filled syringe for ease of administration. The FDA has indicated to us that, along with a PK compatibility study to bridge the vial and syringe navenibart presentation in the Phase 3 program to these new planned devices and human factors testing to support self-administration of these devices, we will need to test one of these device candidates in our Phase 3 program in order for one or both of them to be approved for commercialization. We plan to do this testing in the planned ORBIT-EXPANSE long-term trial. There is no assurance that we will be successful in demonstrating the safety of either of these drug device combinations in the ORBIT-EXPANSE long-term trial, the other required studies or at all, and any such failure would impede our development and commercialization strategy for navenibart. In addition, the FDA or other comparable foreign regulatory authorities could require additional nonclinical studies or clinical trials to support introduction of a drug device combination, which could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase our clinical trial costs, delay marketing approval of navenibart and jeopardize our ability to commence product sales and generate revenue from navenibart, if approved.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, marketing approval and commercialization of navenibart and STAR-0310, which may never occur. If we are unable to develop, or obtain marketing approval for, or, if approved, successfully commercialize navenibart or STAR-0310, we may not be able to generate sufficient revenue to continue our business and our business would be materially harmed.

Interim topline, initial proof-of-concept and preliminary data from our clinical trials that we announce or publish from time to time may change as more study participant data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim topline, initial proof-of-concept or preliminary data from our clinical trials. Interim data or preliminary 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 data become available. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim or preliminary data we previously published. As a result, interim topline, initial proof-of-concept and preliminary data should be viewed with caution until the final data are available. Adverse differences between interim or preliminary data and final data could significantly harm our reputation and business prospects.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials, and results of later stage clinical trials may not enable marketing approval.

The outcome of preclinical studies and early clinical trials, along with interim results from clinical trials, may not be predictive of the success of later clinical trials and may not be supportive of moving into later clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant clinical and regulatory delays or setbacks in late-stage clinical trials after achieving positive interim or final results in preclinical studies or early development, and we cannot be certain that we will not face similar setbacks. The design of a clinical trial can determine whether its results will support advancing into later clinical trials or marketing approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial or trials to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their product candidates. Even if we, or any future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities, as the case may be, may disagree and not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, differences in study design, changes in and adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If we fail to receive positive results in preclinical studies or clinical trials of navenibart, STAR-0310 or any other future product candidate, the development timeline and marketing approval and commercialization prospects for such product candidate, and, correspondingly, our business and financial prospects would be negatively impacted.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome. If clinical trials of a product candidate fail to satisfactorily demonstrate safety and efficacy to the FDA and other comparable foreign regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining approval from the FDA of a biologics license application, or BLA, which would be required for approval of navenibart and STAR-0310, or a new drug application, or NDA. Comparable foreign regulatory authorities, such as the European Medicines Agency, or EMA, require similar approvals. We, and any future collaborators, may never receive such approvals. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy in humans of any product candidate that we may choose to develop before we, or they, will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials we initiate will be conducted as planned or completed on schedule, or at all. In addition, in the case of navenibart, for which we have designed our clinical trials with the goal of demonstrating that it can be dosed in HAE patients every three months and every six months, the length of time to generate sufficient clinical data for registration may necessarily be longer given the length of time between doses in the Phase 3 clinical program. For example, we believe, based on regulatory feedback and the requirements for marketing approvals, that we will need to include data from the ALPHA-ORBIT Phase 3 trial, the ORBIT-EXPANSE long-term trial and the ALPHA-SOLAR trial in our marketing approval applications in order to provide adequate evidence to support an assessment of the every six-month dosing regimen. In addition, we also expect that later stage clinical

trials we conduct for STAR-0310 will be larger and more expensive when compared to those we are conducting for navenibart because AD, the indication for which we are developing STAR-0310, is not a rare disease. Further, the clinical development of product candidates is susceptible to the risk of failure or significant delays at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, failure to utilize clinically appropriate efficacy or safety targets or measurements in a clinical trial for the disease or patient population being studied, failure to have a sufficient number of patients in a clinical trial to establish sufficient safety or efficacy to enable moving into a later stage clinical trial (such as a Phase 3 trial) or marketing approval, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements, failure to enroll a sufficient number of patients on a timely basis or at all, failure to retain a sufficient number of patients to complete any of our trials, determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable, or the need to conduct additional studies or add cohorts to a trial before advancing into the next stage of development. Certain of these risks are heightened in the context of drug development for treatments for rare diseases, in which non-traditional study designs, and often smaller trials are utilized, to demonstrate efficacy and safety, including open-label studies, single arm studies, non-inferiority studies, studies utilizing active comparators or studies utilizing natural history data, biomarkers or other forms of surrogate endpoints, may be utilized due to the challenges inherent in designing and conducting clinical trials for severe diseases with small patient populations. In addition, we may amend the clinical trial protocol to address any issues that we observe as a trial is progressing, including in response to factors impacting safety and the data collected or to adapt the study design to include more clinically appropriate safety or efficacy targets or measurements, or we may be required to make certain changes to clinical trial protocols in response to issues raised by the FDA, the institutional review board, or IRB, other regulatory authorities, investigators or clinical sites. Protocol amendments are subject to IRB and marketing approval before we implement material changes, can result in additional costs, require additional data or participants, and could delay, interrupt, or limit the conduct of the clinical trial. If we terminate or experience delays in the completion of any clinical trials, the commercial prospects for our product candidates may be harmed, and our ability to generate product revenues will be delayed. 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 marketing approval.

It is possible that even if a product candidate that we choose to develop has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in any clinical trials we conduct, we may fail to detect toxicity of or intolerability caused by a product candidate, or mistakenly believe that a product candidate is toxic or not well tolerated when that is not in fact the case. We have not previously submitted a BLA or NDA to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. Moreover, developing biologics is highly complex and any delay or problems in such development, including with third party contract manufacturers that we use to make and develop the drug substance and drug product for our product candidates, may impede our ability to successfully complete clinical development of navenibart or STAR-0310 or any future biologic product candidates we pursue, and obtain FDA approval in a timely manner, if at all. Any inability to complete clinical development successfully could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if (1) we, or any future collaborators, are required to modify our trial designs, such as required modifications with respect to patient populations, endpoints, comparators or trial duration, (2) we, or any future collaborators, are required to conduct additional clinical trials or other testing of a product candidate beyond the trials and testing that we, or they contemplate, (3) we, or any future collaborators, are unable to successfully commence on a timely basis or complete clinical trials of a product candidate or other testing, (4) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or (5) there are unacceptable safety concerns associated with a product candidate, we, or any future collaborators, may:

- be delayed in obtaining marketing approval for such product candidate;
- not obtain marketing approval at all;
- 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 significant safety warnings, including boxed warnings:
- be subject to additional post-marketing testing or other requirements, such as a Risk Evaluation and Mitigation Strategy, or REMS, program; or

- be required to remove the product from the market after obtaining marketing approval.

We may never demonstrate the safety and efficacy of a treatment sufficient to warrant approval for marketing. Our failure to successfully complete clinical trials of a product candidate and to demonstrate the efficacy and safety necessary to obtain approval to market any product candidate would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, a product candidate may be identified during development that could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, a product candidate could cause us, any future collaborators, an IRB or regulatory authorities to interrupt, delay or halt clinical trials of one or more of such product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any such product candidate is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many product candidates that initially showed promise in clinical or earlier stage testing have later been found to cause adverse events or undesirable or unexpected side effects that prevented further development of the product candidates.

If we, or any future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of a product candidate, potential marketing approval or commercialization of such product candidate could be delayed or prevented.

We, or any future collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval or commercialization of a product candidate, including:

- clinical trials may produce unfavorable, inconclusive or insufficient results;
- we, or any future collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials, expand clinical trials or abandon product development programs;
- the number of patients required for clinical trials may be larger than we, or any future collaborators, anticipate, particularly with respect to STAR-0310, which is being developed as a potential treatment for AD which, unlike HAE, is not a rare disease;
- patient enrollment in these clinical trials may be slower than we, or any future collaborators, anticipate, particularly with respect to navenibart, which is being developed as a potential treatment for HAE, a rare disease, which has a significant number of approved products and products in clinical development, including Phase 3 and post-Phase 3 clinical development, or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate or the duration of these clinical trials may be longer than we anticipate;
- the cost of planned clinical trials may be greater than we anticipate;
- our third-party contractors or those of any future collaborators, including those manufacturing such product candidate or components or ingredients thereof, or any drug device combination for a product candidate, such as an autoinjector or pre-filled syringe, or conducting clinical trials on our behalf or on behalf of any future collaborators, may fail to comply with regulatory requirements, program timelines or meet their contractual obligations to us or any future collaborators in a timely manner or at all;
- regulators or IRBs may not authorize us, any future collaborators or our or their investigators to commence, conduct or continue a clinical trial in their regions or countries or may not approve a protocol amendment to an ongoing clinical trial;
- we, or any future collaborators, may have delays in making required submissions to regulatory authorities or IRBs or delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;

- we, or any future collaborators, may have to delay, suspend or terminate clinical trials for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate, or restrictions imposed by applicable governmental authorities due to public health crises, pandemics or epidemics;

- regulators or IRBs may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;

- the FDA or comparable foreign regulatory authorities may disagree or subsequently find fault with our, or any future collaborators', clinical trial designs, including the size of the trials, length of the trials or inclusion or exclusion criteria, or our or their interpretation of data from preclinical studies and clinical trials or may require us to conduct a comparator trial in lieu of a placebo-controlled trial;

- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any future collaborators, enter into agreements for clinical, commercial supplies or drug device combinations for our product candidates;

- we are unable, with our supplier, to develop an autoinjector or pre-filled syringe for navenibart on a timely basis, or to develop and obtain a supplier for suitable delivery device or drug-device combination for any other product candidate for which we seek to develop such a device, that meets the requirements of the FDA or comparable foreign regulatory authorities;

- adequacy of or changes in our manufacturing process or the product formulation or method of delivery;

- the supply or quality of drug product or drug substance, raw materials or other materials necessary to conduct clinical trials may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply;

- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

In addition, we may amend clinical trial protocols to address any issues that we observe as a trial is progressing, including in response to factors impacting safety and the data collected or to adapt the study design to include more clinically appropriate safety or efficacy targets or measurements, or we may be required to make certain changes in response to issues raised by the FDA, IRB, other regulatory authorities, investigators or clinical sites. Protocol amendments are subject to IRB and regulatory approval before we implement material changes, can result in additional costs, require additional data or participants, and could delay, interrupt, or limit the conduct of the clinical trial. If we terminate or experience delays in the completion of any clinical trials, the commercial prospects for our product candidates may be harmed, and our ability to generate product revenues will be delayed. 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.

Product development costs for us, or any future collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of any future product candidate. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical development or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize product

candidates or allow our competitors, or the competitors of any future collaborators, to bring products to market before we, or any future collaborators, do or closer in proximity to the launches of our products or those of our collaborators, and impair our ability, or the ability of any future collaborators, to successfully commercialize product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any future product candidates.

If we, or any future collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our or their receipt of necessary regulatory approvals could be delayed or prevented.

We, or any future collaborators, may not be able to initiate or continue clinical trials for navenibart, STAR-0310 or any other future product candidate if we, or they, are unable to locate and enroll, and maintain the enrollment of, a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any existing or newly approved drugs that may be approved for the indications we are investigating.

Our ability to successfully initiate and complete any clinical trial for navenibart as a potential treatment for HAE, including our ALPHA-ORBIT Phase 3 trial, which we initiated in February 2025, our planned ORBIT-EXPANSE long-term trial, for STAR-0310 as a potential treatment for AD, including the Phase 1a clinical trial we initiated in January 2025, or for any other future product candidate for the potential treatment of any rare disease or any other indication will be dependent upon our ability to enroll, and maintain the enrollment of, a sufficient number of patients with such disease, which will be subject to a number of risks and uncertainties. For example, rare diseases, including HAE, have small patient populations and often have only a limited number of specialist physicians that regularly treat such patients. Further, these specialized sites typically treat a range of diseases and, at any point in time, may have constrained resources and capacity to handle clinical trials. In addition, approved products are available for the treatment of HAE, and additional products may become commercially available during the clinical development of navenibart, and therefore patients and their healthcare providers may feel satisfied with their treatments. As a result, patients may not feel the need to participate in a clinical trial for another product candidate for the same disease or the criteria for the trial may not allow patients on such other therapies to enroll in the trial. Additionally, in the case of HAE, diagnosis is often delayed from onset of symptoms and patients that might be eligible for enrollment in our trials may not have been diagnosed and therefore are unaware of such eligibility. Finally, other companies are and will be conducting clinical trials in HAE, including Phase 3 trials that are already in progress, or may have announced plans for future clinical trials for HAE that are seeking, or are likely to seek, to enroll patients with the disease and patients are generally only able to enroll in a single trial at a time. The small population of patients, competition for these patients and the limited trial sites and their constrained resources may make it difficult for us to enroll enough patients in our clinical trials in HAE, and to maintain the enrollment of enough patients, to complete such clinical trials.

The clinical trials that we may conduct may also have inclusion and exclusion criteria that further limit the population of patients that we are able to enroll. In the case of HAE trials, the inclusion criteria may require that participants have had a certain number of attacks that occur within a defined period of time prior to being able to participate in the trial, which may impact or slow enrollment in

the trial. For example, in the case of our Phase 3 pivotal trial for navenibart, the inclusion criteria require participants to have had a certain number of attacks that occur within a defined period of time prior to being able to participate in the trial, which may impact or slow enrollment in the trial. These inclusion or exclusion criteria could limit the available patient pool and present challenges to clinical trial enrollment.

Our inability, or the inability of any future collaborators, to enroll a sufficient number of patients for any clinical trials, including clinical trials for navenibart as a potential treatment for HAE and clinical trials for STAR-0310 as a potential treatment for AD, that we or they may determine to pursue could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in any such clinical trials may result in increased development costs for the applicable product candidates, delay or halt the development of and approval processes for any future product candidates and jeopardize our, or any future collaborators', ability to commence sales of and generate revenues from any product candidates, which could cause the value of our company to decline.

We have conducted and intend to conduct certain of our clinical trials globally. However, the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans may be delayed, which could materially harm our business.

We have conducted and intend to continue conducting certain of our clinical trials globally. The acceptance by the FDA or other regulatory authorities of data from clinical trials conducted outside their jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice, (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where foreign clinical trial data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the clinical trial is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the trial through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from 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 could result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

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

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

Changes in product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through preclinical studies to later stage clinical trials towards marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are

altered along the way in an effort to optimize processes and results. Any of these changes could cause a product candidate to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, or notification to, or approval by the FDA or a comparable foreign regulatory authority. This could delay completion of clinical trials, require the conduct of bridging clinical trials or studies, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and/or jeopardize our ability to commence product sales and generate revenue.

We face substantial competition from other pharmaceutical and biotechnology companies, and our operating results may suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. If we successfully develop and commercialize any of our product candidates, we and any future collaborators will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Many of the entities developing and marketing potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and commercialization. Even if we are able to successfully develop and commercialize a product, our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than our product.

We are developing navenibart for the potential preventative treatment of HAE. The key competitive factors affecting the success of navenibart, if approved, are likely to be its efficacy, safety, dosing frequency, method of administration, convenience, price and the availability of coverage and reimbursement from government and other third-party payors. In particular, we believe that the competitive position of navenibart will depend in part on whether it is approved for dosing once every three months, once every six months, or both, and whether we are able to obtain commercial approval of dosing with an autoinjector and pre-filled syringe for ease of administration.

In the United States, the FDA has approved four therapies for on-demand treatment of HAE: BERINERT, FIRAZYR, KALBITOR and RUCONEST. For long-term preventative treatment of HAE, the FDA has also approved four therapies: CINRYZE, HAEGARDA, TAKHZYRO and ORLADEYO. There are four main manufacturers of therapies for HAE: CSL Behring (BERINERT and HAEGARDA), Takeda (FIRAZYR, KALBITOR, CINRYZE and TAKHZYRO), Pharming (RUCONEST) and BioCryst (ORLADEYO). With the exception of KALBITOR, these therapies are also approved and commercially available outside of the United States (HAEGARDA is marketed as BERINERT SC outside of the United States). Historically, androgens and antifibrinolytic treatments have also been used as preventative treatment for HAE, however their use is declining with the availability of more-tolerable, HAE-specific therapies.

On-demand and preventative HAE therapies target one of three primary mechanisms. BERINERT, HAEGARDA, RUCONEST and CINRYZE are C1 Esterase Inhibitors (CI-INH) replacement therapies. FIRAZYR is a B2-receptor, or B2R, antagonist, and KALBITOR, TAKHZYRO and ORLADEYO target plasma kallikrein. TAKHZYRO is a monoclonal antibody and ORLADEYO is a small molecule inhibitor.

On-demand therapies are taken as needed; BERINERT and RUCONEST are IV infusions approved for adult and pediatric patients, FIRAZYR is an SC injection, approved for adults 18 and older, and KALBITOR is a series of three SC injections, approved for patients 12 years and older. KALBITOR must be administered by a healthcare professional to monitor for the risk of anaphylactic reactions.

Preventative therapies are taken chronically. CINRYZE is an IV infusion and HAEGARDA is an SC injection; both are administered twice a week and are approved for adult and pediatric patients 6 years and older. TAKHZYRO is an SC injection generally administered every two weeks; however, dosing every four weeks may be considered in some patients. TAKHZYRO is approved for patients 2 years and older.

ORLADEYO is an oral capsule taken once daily with food for patients 12 years and older. Given that TAKHZYRO is an approved monoclonal antibody inhibitor of plasma kallikrein, if navenibart is approved, we expect that it will compete most directly with TAKHZYRO. TAKHZYRO is the current global market leader of HAE preventative treatments.

We are aware of additional programs in development for HAE, which are focused largely on preventative approaches. For example, CSL Behring's garadacimab, a factor XIIa-inhibitory monoclonal antibody, or FXIIa mAb, has completed Phase 3 development for preventative treatment and submitted regulatory applications for marketing approval in regions including the United States. Garadacimab

is approved in the European Union, Australia and the United Kingdom under the brand name ANDEMBRY. Ionis Pharmaceuticals, Inc.'s donidalorsen, an antisense inhibitor of prekallikrein synthesis has also completed Phase 3 development for preventative treatment and has a PDUFA date set for August 21, 2025. Pharvaris is developing two oral treatments, deucrictibant IR (immediate release) and deucrictibant XR (extended release). Deucrictibant is a small molecule inhibitor of B2R. Deucrictibant IR is in Phase 3 development for on-demand treatment. Based on a proof-of-concept Phase 2 trial with deucrictibant IR for preventative treatment, Pharvaris has initiated a Phase 3 trial for deucrictibant XR for preventative treatment. KalVista Pharmaceuticals, Inc. has an oral small molecule plasma kallikrein inhibitor sebetralstat for on-demand treatment of HAE that has completed Phase 3 development and has a PDUFA date set for June 17, 2025 (the Phase 2 trial for KVD824 for preventative treatment was terminated). Intellia Therapeutics has initiated a Phase 3 trial for NTLA-2002, a CRISPR knockout of the prekallikrein gene *KLKB1*. ADARx Pharmaceuticals, Inc. is conducting a Phase 2a trial for ADX-324, a prekallikrein siRNA inhibitor. Argo Biopharmaceutical Co., Ltd. is in Phase 1 development for PKK/BW-20805, an siRNA inhibitor. Preclinical development programs for preventative treatment include KalVista's oral FXIIa inhibitor and Ractigen Therapeutics' C1-INH gene (*SERPING1*) RNA activating program (RAG-12).

We are developing STAR-0310 for the treatment of moderate-to-severe AD. The key competitive factors affecting the success of STAR-0310, if approved, are likely to be its safety and tolerability, efficacy, frequency of dosing, method of administration, convenience, price, and the availability of coverage and reimbursement from government and other third-party payors. In the United States, the FDA has approved two oral JAK inhibitors for the treatment of AD: RINVOQ and CIBINQO, and in the European Union OLUMIANT is also approved for the treatment of AD. Additionally, the FDA has approved four biologics for the treatment of AD: DUPIXENT, ADBRY, EBGLYSS, and NEMLUVIO. Standard of care also includes systemic steroids and topical medications which can treat symptoms but do not address underlying disease. Moderate-to-severe patients who do not respond to topical prescription therapies typically turn to biologics as their next option, and, subsequently, to JAK inhibitors.

Both DUPIXENT and ADBRY are administered subcutaneously every two weeks, and work by targeting the Th2 inflammatory pathway (IL-4/13, and IL-13, respectively). EBGLYSS and NEMLUVIO are administered subcutaneously every two or four weeks, and work by targeting the Th2 inflammatory pathway (IL-13 and IL-31, respectively). RINVOQ and CIBINQO require daily oral administration and are only available to patients who do not sufficiently respond to systemic therapies including biologics. While these JAK inhibitors tend to have better efficacy than the approved biologics, there are significant safety concerns including a boxed warning associated with JAK inhibitors.

We are aware of additional programs in development for AD, which are focused largely on biologic approaches. There are other companies that have product candidates in early-stage development for moderate-to-severe AD, including Nektar Therapeutics (rezpegaldesleukin), Pfizer (PF-07275315 and PF-07264660), LEO Pharma (temtokibart, LEO 152020), Akesobio (AK120), Connect Biopharma (rademikibart), Biosion (bosakitug), Apogee Therapeutics (APG777), InnoCare Pharma (ICP-332), Kymera Therapeutics (KTK-474), GSK (GSK1070806), UCB (UCB9741 and UCB1381), Union Therapeutics (orismilast), J&J (JNJ-7528 and JNJ-5939), Celldex Therapeutics (barzolvolimab), Evommune (EVO301 and EVO756), Eli Lilly (ucenprubart), Sanofi (SAR444656) and Opsidio (OpSCF).

Additionally, a new class of biologics is in clinical development targeting OX40, the same target as for STAR-0310. Amlitelimab (Sanofi) is an anti-OX40 ligand (OX40L) antibody that has started a Phase 3 trial. Rocatinlimab (Amgen) is an afucosylated OX40 receptor (OX40R) antibody currently in Phase 3 trials in AD. IMG-007 (Inmagene) is an OX40 receptor (OX40R) antibody that has completed a proof-of-concept trial in AD. APG990 (Apogee) is an anti-OX40 ligand antibody currently in a Phase 1a trial in AD. ABCL575 (AbCellera) is an anti-OX40 ligand antibody that is in preclinical development.

The enrollment and retention of patients in clinical trials for navenibart or STAR-0310 may be disrupted or delayed as a result of clinicians' and patients' perceptions as to the potential advantages of navenibart or STAR-0310 in relation to commercially available therapies, including approved products as well as any other new products that may be approved in the future, for the treatment of HAE or AD, and competition from clinical trials for other product candidates in development for the treatment of HAE or AD, including with respect to navenibart, competition for enrollment with our ALPHA-ORBIT Phase 3 clinical trial from, among other clinical trials, the Phase 3 trial for Intellia's NTLA-2002 gene editing product candidate for the potential treatment of HAE and Pharvaris's PHVS416 product candidate for the preventative treatment of HAE, both of which began before the ALPHA-ORBIT Phase 3 trial, and CSL Behring's planned garadacimab Phase 4 open-label switch study, which is expected to begin in the first half of 2025.

Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, have fewer or more tolerable side effects, have more convenient dosing regimens, including the potential for biannual or annual dosing regimens, or are less costly than any product candidates that we may develop, which could render any future product candidates obsolete and noncompetitive.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we, or any future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we, or any future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any future collaborators, are able to enter the market.

Our potential future competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and commercializing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, or as a result of the development of drug products that have more convenient dosing regimens. 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.

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

We have limited financial and managerial resources and are focused on the clinical development of navenibart as a potential treatment for HAE, a rare disease with unmet medical need, and the preclinical and clinical development of STAR-0310 as a potential treatment for AD. We would expect that the potential development of STAR-0310 for additional indications, other OX40 development programs and any other future product candidate would also be for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on navenibart, STAR-0310 and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials and we may be unsuccessful in identifying any new product candidates.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support the submission of an IND in the United States, or similar applications in other jurisdictions, including clinical trial application, or CTA, submissions in the European Union. Such studies are complex and may be subject to delays or increased costs due to our dependence upon third parties to assist us with such studies and the ability to source raw materials and the appropriate animals, including non-human primates, so that we can conduct such testing. There is currently a global shortage of non-human primates available for drug development. If the shortage continues, this could increase the cost of conducting our preclinical development and could also result in delays to our development timelines. In the event that the FDA or comparable foreign regulatory authorities require us to complete additional preclinical studies or we are required to satisfy other FDA requests or other requests of comparable foreign regulatory authorities prior to commencing clinical trials, the start of our clinical trials may be delayed or take longer to complete. Even after we receive and incorporate guidance from the FDA or comparable foreign regulatory authorities, such authorities may not agree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or comparable foreign regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications, including CTA submissions in the European Union, will result in the FDA or comparable foreign regulatory authorities allowing clinical trials to begin or that we can meet the requirements imposed by such authorities for beginning such trials on a timely basis or at all.

In addition, any future research programs to identify new product candidates will require substantial technical, financial and human resources, and we may be unsuccessful in our efforts to identify new product candidates. If we are unable to identify suitable additional compounds or biologics for preclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

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

We have never obtained marketing approval for a product candidate. We have not yet succeeded and may never succeed in demonstrating efficacy and safety for any of our product candidates in a Phase 3 clinical trial or in obtaining marketing approval thereafter.

While we intend to submit applications for marketing approval based on data from our Phase 3 clinical program for navenibart if such data are positive, it is nevertheless possible that the FDA, EMA or other applicable foreign regulatory authority may refuse to accept for substantive review any applications that we submit for marketing approval or may conclude after review of our data that our applications are insufficient to obtain marketing approval. If we are able to advance STAR-0310 or any other future product candidate into late-stage development, we would face the same risks with respect to such product candidate. If the FDA, EMA or other applicable foreign regulatory authority does not accept or approve any applications that we submit for marketing approval, they may require that we conduct additional clinical or nonclinical studies, or conduct manufacturing validation studies, and submit that data before they will reconsider our applications. Depending on the extent of these or any other required studies, approval of any application that we submit may be delayed by several years or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA, EMA or other applicable foreign regulatory authority.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing navenibart, STAR-0310 or any future product candidate, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for navenibart, STAR-0310 or any future product candidates, which could significantly harm our business.

If navenibart, STAR-0310 or any other future product candidate receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any future collaborators, to market the drug could be compromised.

Clinical trials of product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that clinical trials for navenibart, STAR-0310 and any other future product candidate, or those of any future collaborator, may indicate an apparent positive effect of such product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur.

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;

- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- we may become the subject of government investigations, which would be expensive to manage and potentially result in the imposition of fines, injunctions or the imposition of civil or criminal penalties;
- the drug may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

Even if navenibart, STAR-0310 or any other future product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for the product candidate may be smaller than we estimate.

Even if navenibart, STAR-0310 or any other future product candidate is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, we believe that the optimal potential commercial success of navenibart as a treatment for HAE will be achieved if we are able to obtain commercial approval at launch for the every three- and six-month dosage regimens. The inability to obtain approvals of both such dosage regimens at launch would likely limit the success of the navenibart launch, limit how rapidly we are able to grow revenues from sales of navenibart, and limit navenibart's overall HAE market share, any of which could have an adverse effect on our results of operations. Similarly, we believe that ease of administration will be a key differentiating factor for navenibart if approved, and, if we are unable to obtain approval of an autoinjector and pre-filled syringe drug device combination in connection with any approval of navenibart, or if any an autoinjector and pre-filled syringe for which we obtain approval is not accepted by patients as a preferred means of administration, the commercial performance of navenibart could suffer. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of future product candidates may require significant resources and may not be successful. If navenibart, STAR-0310 or any other future product candidate is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of navenibart, STAR-0310 or any other future product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to existing approved treatments or alternative treatments, including the frequency, convenience and ease of administration compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy and whether there is an existing standard of care;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;

- the strength of sales, marketing, market access and distribution support;
- the approval of other new products for the same indications;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products in relation to competitive products;
- availability and amount of reimbursement from government payors, managed care plans and other third-party payors, along with any protocols implemented by such entities that require the use of competitive products prior to providing reimbursement for any of our product candidates, if approved;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

The potential market opportunities for product candidates are difficult to estimate precisely. Any estimates we make as to the potential market opportunities for navenibart, STAR-0310 or any other future product candidates will be predicated on many assumptions, including the target product profile, industry knowledge and publications, third-party research reports and other surveys. These assumptions will involve the exercise of significant judgment on the part of our management, will be inherently uncertain and the reasonableness of these assumptions may not have been assessed by an independent source. If any such assumptions prove to be inaccurate, the actual markets for navenibart, STAR-0310 or any other future product candidate could be smaller than our estimates of the potential market opportunities.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any future product candidates that we may develop if and when those product candidates are approved.

We currently do not have a sales, marketing or distribution infrastructure. To achieve commercial success for any approved product, we would need to either develop a sales and marketing organization or outsource these functions to third parties. We expect to use a combination of focused in-house sales and marketing capabilities and third-party collaboration, licensing and distribution arrangements to sell any products that receive marketing approval.

We generally expect that we would seek to retain full commercialization rights in the United States for products that we can commercialize with a specialized sales force and to retain co-promotion or similar rights when feasible in indications requiring a larger commercial infrastructure. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, at such time as we need to, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to a product, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

We generally expect to collaborate or partner with third parties for commercialization outside the United States and both inside the United States and outside the United States for any products that require a large sales, marketing, reimbursement and product distribution infrastructure, such as STAR-0310 if approved for the treatment of moderate-to-severe AD. We would do so through collaboration, licensing and distribution arrangements. As a result of entering into arrangements with third parties to perform sales, marketing, reimbursement and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any product candidates that receive marketing approval.

Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives that could harm our business.

The commercial success of any product that we may develop will depend substantially, both domestically and abroad, on the extent to which the costs of such product will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize such product. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Many countries outside the United States, including many countries in the European Union, require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted and can be lengthy, involve extensive negotiations and potentially result in price caps, significant discounts or other budgetary control measures, which could correspondingly impact pricing and reimbursement in other markets through so-called informal or formal reference pricing schemes. These reviews and negotiations could ultimately result in a pricing and reimbursement structure for a drug that a company deems inadequate and therefore elects not launch in such markets. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if any future product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any product will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for any future products decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

We cannot be sure that coverage will be available for any product candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any product candidate for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Navenibart, STAR-0310 and any other future biologic product candidates will be regulated as biological products, or biologics, and therefore they may be subject to competition from biologic products that are biosimilar to or interchangeable with an FDA-licensed reference biologic product.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biological products that are biosimilar to or interchangeable with an FDA-licensed reference biologic.

Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the licensure 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 develop and receive approval for a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

In December 2022, Congress clarified through the Food and Drug Omnibus Reform Act, or FDORA, that the FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the same first day on which such a product is approved as interchangeable with the reference product and the exclusivity period may be shared amongst multiple first interchangeable products. More recently, in October 2023, the FDA issued its first interchangeable exclusivity determination under the BPCIA.

We believe that our current and any of our future product candidates we develop as biologic products under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once licensed, 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.

Nonetheless, the approval of biosimilar products referencing any of our product candidates would have a material adverse impact on our business due to increased competition and pricing pressures. Moreover, the ultimate impact, implementation and meaning of the BPCIA are subject to uncertainty, and any new regulations, guidance, policies or processes adopted by the FDA to implement the law could have a material adverse effect on the future commercial prospects for our biological products.

For more information on biosimilars and regulatory exclusivity for biologic drugs in the United States, please see the section of this Annual Report on Form 10-K entitled "Business—Government Regulation and Product Approval—Biosimilars and Regulatory Exclusivity."

Business disruptions could delay completion of clinical trials, seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of third-party research institution collaborators, contract research organizations, or CROs, contract manufacturing operations, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, public health crises, pandemics or epidemics, such as the COVID-19 pandemics, and other natural or man-made disasters or business interruptions, for which we may be partly uninsured, as well as impacts of geopolitical events, including civil or political unrest (such as the war between Russia and Ukraine and the conflict in the Middle East), terrorist activity and unstable governments and legal systems. In addition, we expect that we will rely on third-party research institution collaborators for conducting research and development of navenibart, STAR-0310 and any other future product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could delay completion of any clinical trials for such product candidates, seriously harm our operations and financial condition and increase our costs and expenses.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability claims as a result of the clinical testing of product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we or any future collaborators commercially sell any product that we may or they may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of any future product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any future product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain general liability insurance and clinical trial liability insurance that we believe is customary and adequate, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin selling any product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of any future product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Our Financial Position and Need for Additional Capital

We will need substantial additional funding. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We are continuing to conduct clinical trials, preclinical and nonclinical studies, including our Phase 1b/2 ALPHA-STAR trial, which we initiated in February 2023, our ALPHA-SOLAR trial, a long-term open-label clinical trial assessing the long-term safety and efficacy of navenibart, our ALPHA-ORBIT Phase 3 trial of navenibart, which we initiated in February 2025, our planned ORBIT-EXPANSE long-term trial for navenibart, and our Phase 1a clinical trial of STAR-0310 in healthy subjects, which we initiated in January 2025. Additionally, we are continuing to manufacture clinical supplies of navenibart for our ALPHA-ORBIT Phase 3 trial and planned ORBIT-EXPANSE long-term trial, we are ramping up our efforts to manufacture commercial supplies of navenibart for potential commercialization, and are developing drug device combinations for the navenibart Phase 3 program and potential commercialization of navenibart. We expect that our expenses will increase substantially as a result of all of these activities. We will need to raise additional capital in order to fund activities for navenibart beyond our ALPHA-ORBIT Phase 3 trial and other navenibart activities beyond mid-2027, including activities related to the planned ORBIT-EXPANSE long-term trial, drug-device combination development, launch and commercialization activities if we are able to obtain marketing approval for navenibart, and for STAR-0310, for activities beyond our ongoing Phase 1a trial and for any development of STAR-0310 outside of AD. In addition, we may in the future initiate new research, preclinical and clinical development efforts, and seek marketing approval, for other product candidates, and would expect our expenses to increase in connection with each of these activities. If we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator, and these activities would require substantial additional funding. In addition, while we may seek one or more collaborators for future development of our product candidates, we may not be able to enter into a collaboration for any of our product candidates on suitable terms or at all. In any event, our existing cash, cash equivalents and short-term investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Furthermore, we have incurred and will continue to incur significant additional costs associated with operating as a public company.

Accordingly, we will be required to obtain substantial additional funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional funding may not be available to us on acceptable terms, on a timely basis or at all, impacting our ability to execute on our strategic plans. General economic conditions, both inside and outside the United States, including heightened inflation, capital market instability and volatility, interest rate and currency rate fluctuations, and economic slowdown or recession as well as pandemics, epidemics and geopolitical events, including civil or political unrest (such as the war between Ukraine and Russia and the conflict in the Middle East), have resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we could experience an inability to access additional capital. In addition, market volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity. Our failure to raise capital on acceptable terms as and when needed may force us to delay, reduce or eliminate our research and development programs or any future efforts to seek approval for and commercialize products, and would have a material adverse effect on our business, results of operations, financial condition and ability to pursue our business strategy.

Based on our current operating plan, we expect that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into mid-2027. Our current operating plan includes the development of navenibart and STAR-0310, including (i) for navenibart, support for all program activities through completion of our ALPHA-ORBIT Phase 3 trial, including activities related to the planned ORBIT-EXPANSE long term trial and Phase 3 development and testing of drug device combinations for potential dosing of navenibart, and (ii) for STAR-0310, the completion of the ongoing Phase 1a clinical trial of healthy subjects and any related anticipated milestone payments. Our estimate as to how long we expect our cash, cash equivalents and short-term investments to be able to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including:

- our ability to meet our overall timing expectations for navenibart and STAR-0310;
- the progress, timing, costs and results of clinical trials of, and research, preclinical and clinical development, and manufacturing efforts for, navenibart, STAR-0310 and any other future product candidates, including potential future clinical trials and all activities necessary to initiate and conduct clinical trials;
- our ability to enter into and the terms and timing of any additional collaborations, licensing or other arrangements that we may establish;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking marketing approvals;
- the costs of the evaluation, selection, testing and scale up activities related to developing a drug device combination for navenibart, or any other product candidate for which we seek to develop a drug device combination, for late-stage clinical trials and commercialization to the extent such costs are not the responsibility of any future collaborators;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, market access, distribution, supply chain and manufacturing capabilities, scaling up the manufacturing of drug substance and drug product to clinical and commercial scale, securing all raw materials necessary to conduct such scale-up and successfully completing all other activities related thereto;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our product candidates;
- if we obtain marketing approval of any of our products, our ability to successfully compete against other approved products that are approved or used as treatments for the indications for which our products are approved, including with respect to navenibart in HAE and with respect to STAR-0310 in AD;
- our headcount growth and associated costs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

Furthermore, we hold a portion of cash and cash equivalents that we use to meet our working capital and operations expense needs in deposit accounts at one financial institution. The balance in these accounts typically exceed the Federal Deposit Insurance Corporation standard deposit insurance limit of $250,000. If a financial institution in which we hold such funds fails, we could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of such insured funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense obligations.

We have incurred significant losses since inception. We expect to incur losses for at least the next several years and may never achieve or maintain profitability.

Our losses from operations were $111.6 million and $83.0 million for the years ended December 31, 2024 and December 31, 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $674.8 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through private placements of preferred stock before we became a public company and our private placement of preferred stock in February 2021, which we refer to as the February 2021 Financing, registered offerings of our common stock and/or warrants, and our at-the-market offering programs, and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical development programs. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that we will continue to incur significant expenses and operating losses and we may incur increased expenses if and to the extent we:

- initiate and continue research and preclinical and clinical development efforts for navenibart, STAR-0310 and any other future product candidates;
- seek to identify and develop any other future product candidates;
- seek regulatory and marketing approvals for navenibart, STAR-0310 and any other future product candidate that successfully completes clinical trials, in the United States and other markets;
- establish sales, marketing, market access, distribution, supply chain and other commercial infrastructure in the future to commercialize products for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of navenibart, STAR-0310 and any other future product candidates for clinical development and potentially commercialization;
- implement changes in product candidate manufacturing or formulation;
- develop drug device combinations for navenibart, or any other product candidate for which we seek to develop a drug device combination, for late-stage clinical trials and commercialization;
- maintain, expand and protect our intellectual property portfolio; and
- hire and retain additional personnel or add information systems, equipment or physical infrastructure to support our operations.

To become and remain profitable, we or any potential future collaborators must develop and eventually commercialize at least one product candidate with significant market potential. This will require that we or our collaborators be successful in a range of challenging activities, including completing preclinical studies and clinical trials of one or more product candidates, obtaining marketing approval for one or more these product candidates, manufacturing, marketing and selling those products for which we or our collaborators may obtain marketing approval and satisfying any post-marketing requirements. We or our collaborators may never succeed in any or all of these activities and, even if we or our collaborators do succeed, we or our collaborators may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause investors to lose all or part of their investments in us.

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

We will need to raise additional capital to develop and commercialize navenibart and STAR-0310 or to acquire, develop and commercialize any other future product candidates or to pursue other strategic options. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, our existing stockholders' ownership interests may be substantially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. For example, in connection with our acquisition of Quellis Biosciences, Inc., or Quellis, in January 2021 and our February 2021 Financing, we issued an aggregate of 86,077 shares of Series X, of which 53,532 shares of Series X Preferred Stock automatically converted into 8,921,966 shares of our common stock upon the stockholder approval of the conversion of the Series X Preferred Stock into common stock in June 2021. Subsequently, an additional 1,438 shares have converted into 239,608 shares of common stock. The remaining 31,107 shares of Series X Preferred Stock are convertible into 5,184,591 shares of common stock at the election of the holders thereof, subject to certain beneficial ownership limitations. In addition, our June 2018, February 2019 and October 2023 registered offerings of common stock and common stock warrants, which June 2018 and February 2019 warrants have expired, and our January 2020, December 2022 and February 2024 registered offerings of common stock

were highly dilutive to existing stockholders' ownership interests. Further, exercise of the common stock warrants sold in our October 2023 offering could result in additional dilution upon exercise.

Debt financing, if available, would result in periodic payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing additional financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of any future product candidate.

If we raise additional funds through collaborations or marketing, distribution, licensing or royalty arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

We may seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

The development and commercialization of product candidates require substantial cash to fund expenses. We may seek one or more collaborators for the development and commercialization of navenibart, STAR-0310 or any other future product candidates. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. In addition, any collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential collaborations or to otherwise develop specified compounds or biologics.

We face significant competition in seeking appropriate collaborators and strategic partners. Whether we reach a definitive agreement for a collaboration or strategic partnership will depend, among other things, upon our assessment of the other party's resources and expertise, the terms and conditions of the proposed transaction and the proposed party's evaluation of a number of factors. Those factors may include the potential differentiation of ours or a partner's product candidate from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator or strategic partner may also be considering alternative transaction types and structures that may be more attractive than the one with us.

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

If we enter into collaborations with third parties for the development and commercialization of a product candidate, our prospects with respect to such product candidate will depend in significant part on the success of those collaborations.

If we enter into collaborations for the development and commercialization of a product candidate, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of such product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon

research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. Collaborations involving product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of a product candidate or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the market or competitive landscape, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in negative publicity for our product candidate and the need for additional capital to pursue further development or commercialization of the applicable product candidates.

In addition, all of the risks related to product development, marketing approval and commercialization described in this "Risk Factors" section would apply to the activities of our collaborators. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination or a sale or other transaction involving our collaboration, it or the party with which it entered into a business combination, sale or other transaction could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

We rely on third parties to conduct our preclinical studies and clinical trials. If they do not perform satisfactorily, our business could be significantly harmed.

We rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct ongoing and planned preclinical studies and clinical trials of navenibart, STAR-0310 or any other future product candidates. Any of these third parties could terminate its engagement with us under certain circumstances or encounter, for example, business challenges, such as a loss of business, public health crises, pandemics or epidemics, such as the COVID-19 pandemic, or the impacts of geopolitical events, including civil or political unrest (such as the war between Russia and Ukraine and the conflict in the Middle East), or enter into transactions, such as business combinations, that temporarily or permanently impact the amount or type of resources that they are able or willing to devote to our engagement. We might not be able to enter into alternative arrangements or do so on commercially reasonable terms or on a timely basis. In addition, there is a natural transition period when a new CRO begins work. As a result, delays would likely occur, which could materially impact our ability to meet our expected preclinical and clinical development timelines and harm our business, financial condition and prospects.

Further, our reliance on these third parties for preclinical and clinical development activities limits our control over these activities, but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a CRO for a trial of a product candidate, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and most other comparable regulatory authorities outside the United States require us to comply with standards, commonly referred to as current GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA and other comparable regulatory authorities outside the United States enforce these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or any of our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other comparable regulatory authorities outside the United States may require us to perform additional clinical trials before approving a product candidate, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA or other comparable regulatory authorities outside the United States will determine that any of our clinical trials comply with GCPs. Similar standards, known as Good Laboratory Practices, apply to preclinical studies and nonclinical trials and other studies. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Other regions, including the European Union, have similar requirements. The failure to comply with these registration and posting requirements can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties that conduct preclinical studies and clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we are not able to control whether or not they perform satisfactorily or devote sufficient time, skill and resources to our development programs. Any such contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our preclinical and clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for the applicable product candidates. If that occurs, we would not be able to, or may be delayed in our efforts to, successfully commercialize such product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be impaired.

We also rely on other third parties to store and distribute drug supplies for any clinical trials we pursue. Any performance failure on the part of any such distributors or impacts from geopolitical events, including civil or political unrest (such as the war between Ukraine and Russia and the conflict in the Middle East), terrorist activity and unstable governments and legal systems could delay clinical development or marketing approval of any future product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

The manufacturing of pharmaceutical products and, in particular, biologics, is complex and we do not have our own manufacturing capabilities. We rely and intend to rely on third parties to produce preclinical, clinical and commercial supplies of our current and future product candidates as well as the device candidates that we intend to commercialize with our product candidates.

We currently have no manufacturing facilities and rely on third-party contract manufacturers to manufacture our cell banks, all of our preclinical product candidate supplies, clinical trial product candidate supplies and drug device combination supplies, and will need to rely on third-party contract manufacturers to manufacture commercial supply of any products or drug device combinations for which we may obtain marketing approval. We do not own, nor do we plan to own, any manufacturing facilities. There can be no assurance that our preclinical, clinical and commercial development product supplies, including drug substance, drug product, drug device combinations, or the master cell bank for STAR-0310, that are being manufactured by third parties will not be delayed, limited or interrupted, or be of satisfactory quality or continue to be available at acceptable prices. Additionally, the process of manufacturing pharmaceutical products, devices and, in particular, biologics is complex, highly regulated, and subject to multiple risks. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics, difficulties in scaling the production process and use of excipients which may, among other things, impact shelf life and present concerns with process controls. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, other supply disruptions and higher costs. If microbial, viral or other contaminations are discovered at the facilities of our third-party contract manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials, result in higher costs of drug product and adversely affect our business.

If the contract manufacturers we engage are unable to supply us with sufficient preclinical or clinical quality and quantities of our product candidates, or drug device combinations for our product candidates, and we are unable to timely establish an alternate supply from one or more third-party contract manufacturers, we will experience delays in our development efforts as we seek to locate and qualify new or additional manufacturers. In particular, any replacement of our third-party contract manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements or capacity could be limited at each of the qualified replacements. We generally rely on single source third-party manufacturers and suppliers for the antibodies used to make navenibart and STAR-0310 drug substance and drug product, to label and pack navenibart, and to supply our drug device combinations of navenibart, and we expect to continue to do so to meet our nonclinical, clinical and commercial needs for navenibart, STAR-0310, and any other product candidate, which exacerbates these and other related risks for us. In addition, in connection with preparing for the potential commercialization of navenibart, we plan to transition to a new third-party contract manufacturer to produce the commercial supply of navenibart. While we believe that we can make this transition without affecting our expected timelines or the availability of commercial supply, we cannot be certain that we will be able to do so. Additionally, contract manufacturers may rely on single source suppliers for certain of the raw materials or drug or device components for our preclinical and clinical product supplies. We may be unable to obtain raw materials or drug or device components for an indeterminate period of time if any of our third-party suppliers or manufacturers were to cease or interrupt production or otherwise fail to supply these materials or components to us for any reason, including due to trade barriers, import/export controls or other legal restrictions or limitations; regulatory requirements or actions (including recalls), adverse financial developments at or affecting the supplier or manufacturer, failure by the supplier or manufacturer to comply with current good manufacturing practices, or cGMPs, contaminations, business interruptions, or labor shortages or disputes, or if we were to terminate our relationship with any of our third-party suppliers or manufacturers for any reason. Suppliers may extend lead times, limit supplies or increase prices due to capacity constraints or other factors beyond our control. We cannot be sure that single source suppliers for our raw materials or drug or device components will remain in business or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these raw materials or components for our intended purpose. If current or future suppliers are delayed or unable to supply sufficient raw materials or components to manufacture product for our preclinical studies and clinical trials, we may experience delays in our development efforts as materials are obtained or we locate and qualify new raw material manufacturers.

The manufacturing processes for clinical candidates and drug device combinations are subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with their standards, such as cGMPs. In the event that any of our manufacturers fail to comply with such requirements or to perform their obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third-party, which we may not be able to do on reasonable terms or on a timely basis, if at all. The transfer of the manufacturing of biologic products to a new contract manufacturer and any additional process development that may be necessary can be lengthy and involve

significant additional costs. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer would negatively affect our ability to develop product candidates in a timely manner or within budget.

Further, our reliance on third-party manufacturers exposes us to risks beyond our control, including the:

- inability to meet our drug specifications, quality requirements or drug device combination requirements consistently;
- inability to initiate or continue preclinical studies or clinical trials of product candidates or drug device combinations under development;
- delay or inability to procure or expand sufficient manufacturing capacity;
- costs and validation of new equipment and facilities required for scale-up;
- inability of our third-party manufacturers to execute process development, manufacturing, technology transfers, manufacturing procedures and other logistical support requirements appropriately or on a timely basis;
- inability to scale-up manufacturing while maintaining appropriate quality control;
- failure to comply with cGMPs and similar foreign standards;
- reliance on a limited number of sources, and in some cases, potentially single sources for drug or device components and raw materials, such that if we are unable to secure a sufficient supply of these drug or device components and raw materials, we will be unable to manufacture and sell our future product candidate in a timely fashion, in sufficient quantities or under acceptable terms;
- price increases or decreased availability of drug or device components or raw materials;
- lack of qualified backup suppliers for those components and raw materials that are purchased from a sole or single source supplier;
- inability to negotiate development and manufacturing agreements with third parties under commercially reasonable terms, if at all;
- breach, termination or nonrenewal of development and manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- disruption of operations of our third-party manufacturers or suppliers by conditions unrelated to our business or operations, including supply chain issues, capacity constraints, transportation and labor disruptions, global competition for resources, the bankruptcy of the manufacturer or supplier, a business combination or strategic transaction involving the manufacturer or supplier, the issuance of an FDA Form 483 notice or warning letter and/or general economic conditions, heightened inflation, interest rate and currency rate fluctuations, and economic slowdown or recession;
- disruptions of operations caused by geopolitical events, including trade barriers, civil or political unrest (such as the war between Ukraine and Russia and the conflict in the Middle East), terrorist activity, insurrection or other wars or significant conflicts, unstable governments and legal systems man-made or natural disasters or public health crises, pandemics and epidemics, including, for example, the COVID-19 pandemic;
- carrier disruptions or increased costs that are beyond our control, including increases in material, labor or other manufacturing-related costs or higher supply chain logistics costs;
- failure to deliver our drugs under specified storage conditions and in a timely manner; and

- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production, any of which could result in a failure to begin our clinical trials or having to stop or delay ongoing clinical trials. In addition, our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of the regulatory action, our preclinical, clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

Our contract manufacturers are or may be engaged with other companies to supply and manufacture materials or products for such companies, which further exposes our suppliers and manufacturers to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or manufacturer's facility, which could impact the contract supplier's or manufacturer's ability to manufacture for us.

In addition, a material shortage, contamination, recall or restriction on the use of substances in the manufacture of our product candidates or drug device combinations for our product candidates, or the failure of any of our key suppliers to deliver necessary components required for the manufacture of our product candidates or drug device combinations for our product candidates, could adversely impact or disrupt the commercial manufacture or the production of preclinical or clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations, and future prospects.

Any of these events could lead to preclinical study or clinical trial delays or failure to obtain marketing approval or impact our ability to successfully commercialize our current or any future product candidates if approved.

Changes in U.S./China trade policies may adversely impact our business and operating results.

We are utilizing a Chinese contract development and manufacturing organization for the process and product development for navenibart and STAR-0310 and the U.S. and Chinese governments have in recent years taken or otherwise proposed a number of actions to restrict trade between the two countries, including imposing several rounds of tariffs and, in the case of the U.S. government, calling for investigations into and the imposition of possible economic sanctions against Chinese biotechnology companies and the proposal of the BIOSECURE Act, which targets certain Chinese biotechnology companies.

As a result, we are exposed to the possibility of product supply disruption and increased costs and expenses in the event of further escalation of trade restrictions between the United States and China.

Any such unfavorable government policies with respect to U.S./China trade, such as export controls, capital controls or tariffs, may increase the cost of manufacturing our product candidates or drug device combinations for our product candidates, affect the demand for our drug products or drug device combinations (if and once approved), the competitive position of our product candidates or drug device combinations for our product candidates, and import or export of raw materials and finished product candidate or drug device combinations for our product candidates used in our preclinical studies and clinical trials, any of which could have an adverse effect on our business, financial condition and results of operations.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to commercialize such product candidates successfully may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to navenibart, STAR-0310 and any other future product candidates. If we do not adequately protect our intellectual property, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. See the section "Business — Intellectual Property" for more details regarding our navenibart and STAR-0310 patent portfolios. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Failure to protect or to obtain, maintain or

extend adequate patent and other intellectual property rights could materially adversely affect our ability to develop and market our products and product candidates. The enforcement, defense and maintenance of such patents and other intellectual property rights may be challenging and costly.

We cannot be certain that any patent application directed to our current or future product candidates will be issued in a form that provides us with adequate protection to prevent competitors from developing competing products. As a biopharmaceutical company, our patent position is uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biopharmaceutical patents. Consequently, patents may not issue from any applications that are currently pending or that we file in the future. As such, we do not know the degree of future protection that we will have for our product candidates and their use. The scope of patent protection that the USPTO and foreign patent offices will grant with respect to our product candidates is uncertain. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. For example, it is possible that the USPTO and foreign patent offices will not allow broad antibody claims that specifically cover our navenibart and STAR-0310 product candidates and antibodies closely related to them. As a result, upon receipt of FDA approval, or marketing approval in foreign jurisdictions, competitors may be free to market antibodies almost identical to ours, including biosimilar antibodies, thereby decreasing our market share. However, a competitor cannot submit to the FDA an application for a biosimilar product based on navenibart, STAR-0310 or any future biologic products until four years following the date of approval of our "reference product," and the FDA may not approve such a biosimilar product until 12 years from the date on which the reference product was approved. See the section "Business — Government Regulation and Product Approval — Biosimilars and Regulatory Exclusivity" for more details regarding biosimilar regulatory exclusivities.

Our owned and in-licensed pending patent applications and any future patent applications we file cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, patents are granted to the party who was the first to file a patent application. However, prior to March 16, 2013, in the United States, patents were granted to the party who was the first to invent the claimed subject matter. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third party preissuance submission of prior art to the USPTO, or become involved in post-grant review procedures, oppositions, derivations, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing antibodies or compounds similar or identical to our product candidates, or limit the duration of the patent protection of our product candidates. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Patent applications may not result in patents being issued which protect any current and future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does.

Even if patent applications that we file issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with any of our future products. Alternatively, our competitors may seek to market biosimilar versions of any approved products by submitting an application for a biosimilar product under the BPCIA. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents

invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

If we do not obtain protection under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, and similar non-United States legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Patents have a limited duration. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest United States non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, their manufacture, or use are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our United States patents, if issued, may be eligible for limited patent term extension under the Hatch-Waxman Act, or under similar legislation in other countries. The Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. The patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner than we expect. As a result, our revenue from applicable products could be reduced, possibly materially.

We rely on in-licensed patent and other intellectual property rights for our STAR-0310 program and we may need to obtain licenses from third parties to other intellectual property rights for the development and commercialization of our STAR-0310 and navenibart programs; if we fail to comply with our existing or future obligations under these licenses, or if these licenses are terminated, we could lose license rights that are important to our business.

Our ability to develop and commercialize our STAR-0310 program is heavily dependent on an in-license to patent rights and other intellectual property granted to us by Ichnos. In October, 2023, we entered into the Ichnos License Agreement, pursuant to which Ichnos granted us an exclusive (even as to Ichnos and its affiliates), worldwide, and sublicensable right and license to certain patent rights and related know-how to develop, manufacture, and commercialize Ichnos' proprietary OX40 portfolio. The OX40 portfolio includes Ichnos' proprietary OX40 antagonist monoclonal antibody, with the generic name telazorlimab and also referred to by Ichnos as "ISB 830" as well as Ichnos' proprietary affinity matured next generation OX40 antagonist monoclonal antibody referred to by Ichnos as "ISB 830-X8". We are developing STAR-0310, which was engineered from ISB 830-X8 with YTE half-life extension technology modification, for AD and potentially for other allergic and immunological diseases. STAR-0310 is currently in preclinical development. Ichnos has also agreed not to develop or commercialize any product that directly modulates the OX40 receptor.

Under the Ichnos License Agreement, we agreed to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one product that contains or comprises a licensed compound in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. The Ichnos License Agreement imposes on us payment of development, regulatory and commercial milestones, as well as tiered royalties and other obligations. If we fail to comply with our obligations under the Ichnos License Agreement, or we are subject to a bankruptcy, Ichnos may have the right to terminate the license, in which event we would not be able to market products covered by the agreement. Our business could suffer, for example, if the Ichnos License Agreement terminates, if Ichnos fails to abide by the terms of the license, or if the licensed patents or other rights are found to be invalid or unenforceable.

In the future, we may need to obtain licenses to intellectual property rights necessary to develop and commercialize our product candidates, including navenibart and STAR-0310, or may need to amend existing or future licenses. If we are unable to obtain or amend

such licenses at a reasonable cost or on reasonable terms, we may be unable to develop or commercialize our product candidates, which could harm our business significantly.

As noted above, the Ichnos License Agreement imposes, and we expect that future license agreements will impose, diligence obligations, milestone and royalty payments, indemnification and other obligations on us. If we fail to comply with our obligations under one or more of these licenses, our licensors, including Ichnos, may have the right to terminate the license agreement at issue. If one or more of these licenses is terminated, we may be unable to develop or commercialize our product candidates, including navenibart and STAR-0310. Termination of any of our current or future license agreements or reduction or elimination of our licensed rights may require us to negotiate new or reinstated licenses with less favorable terms, even if available at all.

In addition, our license agreements are, and future license agreements are likely to be, complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of the licensed rights, or increase what we believe to be our diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over the license agreements or the in-licensed intellectual property prevent or impair our ability to maintain our current license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidate. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

License agreements we may enter into in the future may be non-exclusive, or may not include all territories or fields of use of interest to us. Accordingly, third parties may also obtain licenses from such licensors to the same intellectual property rights they have licensed to us. As a result, the licenses granted to us may not provide us with exclusive rights to use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our product candidates, which may permit competitors to develop and commercialize a competitive product.

Furthermore, in some cases, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we in-license from third parties. Therefore, we cannot be certain that any in-licensed patent rights will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our future licensors or collaboration partners fail to obtain, maintain or protect any patents or patent applications licensed to us, decide not to pursue litigation against third-party infringers, fail to prosecute infringement, or fail to defend against counterclaims of patent invalidity and unenforceability, our rights to such patents and patent applications may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected.

Disputes may arise among us and our current and future licensors regarding intellectual property subject to a licensing agreement, including:

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

If disputes over intellectual property that we have licensed, or license in the future, prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

An intellectual property litigation could lead to unfavorable publicity that could harm our reputation and cause the market price of our common stock to decline.

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. In such event, the market price of our common stock may decline.

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

Our commercial success depends, in part, on our ability to develop, manufacture, and market our current as well as any future product candidates, without infringing the intellectual property and other proprietary rights of third parties. If any third-party patents or patent applications are found to cover our current or any future product candidates or their methods of use, or other aspects of our current or future product candidates, we may not be free to manufacture or market such product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all, or we may incur significant legal fees or damages.

In spite of our efforts to avoid obstacles and disruptions arising from third-party intellectual property, it is impossible to establish with certainty that our programs directed to our current and any future product candidates will be free of claims by third-party intellectual property holders. Even with modern databases and on-line search engines, literature searches are imperfect and may fail to identify relevant patents and published applications. Even when a third-party patent is identified, we may conclude upon a thorough analysis, that we do not infringe the patent or that the patent is invalid. If the third-party patent owner disagrees with our conclusion and we continue with the business activity in question, patent litigation may be initiated against us. Alternatively, we might decide to initiate litigation in an attempt to have a court declare the third-party patent invalid or non-infringed by our activity. In either scenario, patent litigation typically is costly and time-consuming, and the outcome is uncertain. The outcome of patent litigation is subject to uncertainties that cannot be quantified in advance, for example, the credibility of expert witnesses who may disagree on technical interpretation of scientific data. Ultimately, in the case of an adverse outcome in litigation, we could be prevented from commercializing a product or using certain aspects of our technology platform as a result of patent infringement claims asserted against us. This could have a material adverse effect on our business.

There is a substantial amount of intellectual property litigation in the biopharmaceutical industry, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our current or future product candidates, including interference proceedings before the USPTO. Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The biopharmaceutical industry has produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that any current or future product candidates, products, methods, processes, modeling or similar work either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. For example, we are aware of a U.S. patent directed to an antibody that binds plasma kallikrein. In the event that the owner of this patent were to bring an infringement action against us, we may have to argue that navenibart, its manufacture or use does not infringe a valid claim of this patent. We cannot guarantee that a court would find in our favor on questions of infringement or validity. Furthermore, even if our arguments are successful, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing any future product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Our involvement in litigation, and in, e.g., any interference, derivation, reexamination, inter partes review, opposition or post-grant proceedings or other intellectual property proceedings in the United States, or other jurisdictions, may divert management time from focusing on business operations, could cause us to spend significant amounts of money and may have no guarantee of success. Any current and potential intellectual property litigation also could force us to do one or more of the following:

- stop selling, manufacturing or using our products in the United States or other jurisdictions that use the subject intellectual property;
- obtain from a third party asserting its intellectual property rights, a license to sell or use the relevant technology, which license may not be available on reasonable terms, or at all, or may be non-exclusive thereby giving our competitors access to the same technologies licensed to us;
- redesign those products or processes that use any allegedly infringing or misappropriated technology, which may result in significant cost or delay to us, or which redesign could be technically infeasible; or
- pay damages, including the possibility of treble damages in a patent case if a court finds us to have willfully infringed certain intellectual property rights.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

Along with patent protection, we also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing processes. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, CROs, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants.

Trade secrets and confidential know-how are difficult to maintain as confidential. Although we use reasonable efforts to protect our trade secrets, any party with whom we have executed a confidentiality agreement may breach that agreement and disclose our proprietary information, including our trade secrets.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Accordingly, we may not be able to obtain adequate remedies for such breaches, despite any legal action that we might take against persons making such unauthorized disclosures. In addition, courts outside the United States sometimes are less willing than United States courts to protect trade secrets.

If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

Those with whom we collaborate on research and development related to current and future product candidates may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the United States and other countries could increase those uncertainties and costs. For example, the Leahy-Smith America Invents Act of 2011, or the Leahy-Smith Act, included a number of significant changes to United States patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, for example, via post grant review and inter partes review proceedings at the USPTO. In addition, the Leahy-Smith Act transformed the United States patent system into a "first to file" system. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The United States Supreme Court has ruled on several patent cases, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations; including the scope of patent protection for antibodies. Additionally, there have been proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the Congress, the United States courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make antibodies that are the same as or similar to navenibart, STAR-0310 or any other future product candidates but that are not covered by the claims of patents that we own or have rights to;

- we or our licensors or any current or future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by our pending patent application;

- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent rights will not lead to issued patents, or that patents, if granted, may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our products or technologies could use the intellectual property of others without obtaining a proper license;
- we may not develop additional technologies that are patentable; and
- third parties may allege that our development and commercialization of navenibart, STAR-0310 or any other future products may infringe their intellectual property rights, the outcome of which may have an adverse effect on our business.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering any future product candidates, our competitive position would be adversely affected.

We may obtain only limited geographical protection with respect to certain patent rights, which may diminish the value of our intellectual property rights in those jurisdictions and prevent us from enforcing 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. Accordingly, we may not file for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national/regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The requirements for patentability may differ in certain countries, particularly in developing countries. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents or where any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing with us.

In addition, our ability to protect and enforce our intellectual property rights may be adversely affected by changes in foreign intellectual property laws. For example, the European Union opened a Unified Patent Court, or UPC, in June 2023. The UPC is a common patent court that hears patent infringement and revocation proceedings effective for member states of the European Union. This could enable third parties to seek revocation of any of our European patents, should they be granted, in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated. Any such revocation and loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates. Moreover, the controlling laws and regulations of the UPC will develop over time, and may adversely affect our ability to enforce our European patents or defend their validity. We may decide to opt out our patent applications, if filed, and our European patents, if granted, from the UPC. If certain formalities and requirements are not met, however, our European patent applications, if filed, and European patents, if granted, could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that our European patent applications or granted patents will avoid falling under the jurisdiction of the UPC, even if we decide to opt out of the UPC.

Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business, results of operations and financial condition may be adversely affected. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities in those jurisdictions is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we may not be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property or claiming ownership of what we regard as our own intellectual property.

Many of our employees, including our senior management, were previously employed at other biopharmaceutical companies, including our competitors or potential competitors. Some of these employees, including members of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Risks Related to Marketing Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of navenibart, STAR-0310 or any other future product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of biopharmaceutical products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, which regulations differ from country to country. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we, or they, receive approval of a BLA from the FDA, which would be required for approval of navenibart and STAR-0310, or NDA or marketing approval from applicable regulatory authorities outside the United States. Product candidates in the development phase are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have no experience as a company in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third parties, including third-party clinical research organizations, to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. The FDA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

We will need to carefully review the guidance and advice that FDA and other regulatory and scientific authorities in foreign jurisdictions, including the Committee for Medicinal Products for Human Use, or CHMP, provide in any meetings we have with those authorities to discuss our clinical development program. Sponsors are given opportunities to meet with the FDA and other regulatory bodies at certain points in their clinical development programs. At the conclusion of these meetings, the FDA and comparable regulatory authorities will provide responses to questions posed by the sponsor regarding the clinical development program. They will not indicate whether an application will be approved, but will provide guidance to the sponsor on various questions, including what types of studies and data are likely necessary to support review and approval of an NDA, BLA or marketing authorization. For example, the FDA may express support for the sponsor's approach in the clinical development program but indicate that questions concerning whether the data support approval will be subject to review by the agency following its acceptance for filing of the NDA or BLA. While such guidance is not legally binding, our failure to carefully consider these recommendations for the design of a clinical program may put the program at significant risk of failure.

Further, the FDA may determine that we must provide additional evidence of safety or efficacy before approving a BLA or NDA for our product candidates. For example, the FDA reviews an application to determine whether there is "substantial evidence" to support a finding of effectiveness for the proposed product for its intended use(s), The FDA has interpreted this evidentiary standard to generally require at least two adequate and well-controlled clinical trials to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional confirmatory evidence may satisfy this standard. The FDA issued draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical trial to demonstrate efficacy. In the event that we submit a BLA or NDA on the basis of one clinical trial and confirmatory evidence, the FDA could determine that such information is not sufficient to support approval of the application and the agency could require us to conduct an additional trial in support of the BLA or NDA.

In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of FDORA, Congress required sponsors to develop and submit a Diversity Action Plan, or DAP, for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On

January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

Further, in January 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. This regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one European Union Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the European Union Member States and the public. We plan to seek approval of the ALPHA-ORBIT Phase 3 trial and ORBIT-EXPANSE long-term trial in the European Union pursuant to this regulation, but there is no assurance that we will be able to secure such an authorization for our ongoing or future clinical trials of navenibart, STAR-0310 or any future product candidates.

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

Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Further, under the Pediatric Research Equity Act, or PREA, an NDA or BLA, or supplement to an NDA or BLA, for certain drugs and biological products must contain data to assess the safety and efficacy of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the European Union also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the EMA or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking marketing approval in the United States or the European Union, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the court overruled *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc*., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

Any delay in obtaining or failure to obtain required approvals could negatively affect our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we may be granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions and any of our product candidates that may be approved for marketing in a foreign jurisdiction will be subject to risks associated with foreign operations.

In order to market and sell our products in the European Union and other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize our products in any market.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-United States marketing approvals and compliance with non-United States regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we fail to obtain the non-United States approvals required to market our product candidates outside the United States or if we fail to comply with applicable non-United States regulatory requirements, our target markets will be reduced and our ability to realize the full market potential of our product candidates will be harmed and prospects may be adversely affected.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom as a result of the withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure, or IPR, will apply, which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EU/European Economic Area, or EEA, member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any approvals may force us or our collaborators to restrict or delay efforts to seek marketing approval in the UK for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, European Union pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (among other things, potentially reducing the duration of regulatory data protection and revising the eligibility for expedited pathways) was published in April 2023. The proposed revisions

remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets (such as the war between Ukraine and Russia and the conflict in the Middle East); compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

We, or any future collaborators, may not be able to obtain or maintain orphan drug designation or orphan drug exclusivity for any future product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We, or any future collaborators, may seek orphan drug designations and may be unable to obtain such designations. Navenibart was granted orphan drug designation by the FDA and orphan medicinal product designation by the EMA for the treatment of HAE.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because FDA has taken the position that, under certain circumstances, another drug with the same active moiety can be approved for the same condition. Specifically, the FDA's regulations provide that it can approve another drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

In 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA, which among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by FDA.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use."

Although there have been legislative proposals to overrule this decision, they have not been enacted into law. In January 2023, the FDA announced that, in matters beyond the scope of the court's order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. We do not know if, when, or how the FDA or Congress may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our

business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

In addition, to obtain and maintain orphan drug designation in the European Union, we would need to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the medicinal product will be of substantial benefit to those affected by that condition. There is no assurance that we would be able to meet that standard for any product candidate. In particular, while we have obtained orphan drug designation for navenibart for the treatment of HAE in the European Union, we will not be able to maintain that designation if we are not able to show, to the satisfaction of European Union regulatory authorities, that navenibart is of substantial benefit to HAE patients over available commercial products for HAE in the European Union and the additional products that are ahead of navenibart in clinical development for HAE.

Any product candidate for which we obtain marketing approval would remain subject to ongoing regulation and could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements, when and if any of our product candidates are approved.

Any product candidate for which we obtain marketing approval will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a REMS. Accordingly, if we receive marketing approval for one or more of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

We must also comply with requirements concerning advertising and promotion for any product candidate for which we obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Violations of the Federal Food, Drug, and Cosmetic Act, or FDCA, and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

We will also need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products. In September 2021, the FDA published final regulations which describe the types of evidence that the Agency will consider in determining the intended use of a drug or biologic. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

In addition, later discovery of previously unknown adverse events or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;

- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions. Further, the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union, notably under Directive 2001/83EC, as amended, and are also subject to European Union Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the European Union.

Accordingly, assuming we, or any future collaborators, receive marketing approval for one or more of our product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, our or any future collaborators' ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

We may seek certain designations for our product candidates, including Breakthrough Therapy, RMAT Therapy, Fast Track and Priority Review designations in the United States, and the PRIority MEdicines, or PRIME, designation in the European Union, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy and Regenerative Medicine Advanced Therapy, or RMAT, product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough and RMAT 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.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The FDA has granted Fast Track designation to navenibart for the treatment of HAE.

We may also seek a Priority Review designation for one or more of our product candidates. If the FDA determines that a product candidate would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may, among other things, later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

In the European Union, we may seek PRIME designation for some of our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the European Union or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the European Union and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

We may seek approval of our product candidates from the FDA or comparable foreign regulatory authorities through the use of accelerated development pathways. If we are not able to use such pathways, we may be required to conduct additional clinical trials beyond those that are contemplated, which would increase the expense of obtaining, and delay or prevent the receipt of, necessary marketing approvals. Moreover, even if we receive accelerated approval from the FDA or comparable foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA or comparable foreign regulatory authorities may seek to withdraw accelerated approval.

Under the FDCA and implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit. Prior to seeking such accelerated approval, we will continue to seek feedback from the FDA or comparable foreign regulatory agencies and otherwise evaluate our, or their, ability to seek and receive such accelerated approval.

There can be no assurance that the FDA or foreign regulatory agencies will agree with our surrogate endpoints or intermediate clinical endpoints in any of our clinical trials, or that we will decide to pursue or submit any additional NDAs or BLAs seeking accelerated approval. Similarly, there can be no assurance that, after feedback from the FDA or comparable foreign regulatory agencies, we will continue to pursue or apply for accelerated approval. Furthermore, for any submission of an application for accelerated approval, there can be no assurance that such submission will be accepted for filing or that any expedited development, review or approval will be granted on a timely basis, or at all.

Finally, there can be no assurance that we will satisfy all FDA requirements, including new provisions, that govern accelerated approval. For example, with passage of the FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to the FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing the FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that qualifies for accelerated approval.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology In therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

In the European Union, a "conditional" marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a "standard" marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed.

Accordingly, a failure to obtain and maintain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period until commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We may seek a Rare Pediatric Disease priority review voucher, or PRV, for our current and future product candidates. A BLA or NDA for our current and future product candidates will not, however, meet the eligibility criteria for a PRV, unless this program is reauthorized by Congress and we secure rare pediatric disease designation and approval of the BLA or NDA for the product candidate before any required dates established in such legislation.

With enactment of the Food and Drug Administration Safety and Innovation Act of 2012 and subsequent legislation, Congress authorized the FDA to award PRVs to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives approval for a new drug or biologic for a rare pediatric disease may qualify for a PRV, which can be redeemed for priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product that receives a PRV may transfer, including by sale, the PRV to another sponsor and that PRV may be further transferred any number of times before it is used. A PRV entitles the holder to designate a single

human drug application submitted under Section 505(b)(1) of the FDCA or Section 351 of the Public Health Service Act as qualifying for a priority review. An FDA priority review may expedite the review process of a marketing application reducing the review time from ten months after formal acceptance of the file to six months after formal acceptance of the file.

In order for a sponsor to receive a PRV in connection with approval of a BLA or NDA, the investigational product must be designated by the FDA as a product for a rare pediatric disease prior to submission of the marketing application. A rare pediatric disease is a disease that is serious or life-threatening and which primarily affects individuals aged from birth to 18 years and fewer than 200,000 people in the United States. Alternatively, the disease may affect more than 200,000 people in the United States if there is no reasonable expectation that the cost of developing and making available in the United States a product for such disease or condition will be recovered from sales in the United States of such product. In addition, to qualify for a PRV, the sponsor must request the voucher and the BLA or NDA must itself be given priority review, rely on clinical data derived from studies examining a pediatric population and dosages of the product intended for that population, not seek approval for a different adult indication in the original rare pediatric disease product application and be for a product that does not include a previously approved active ingredient.

Under the statutory sunset provisions for the Rare Pediatric Disease PRV Program, the FDA was authorized to award a PRV for an approved rare pediatric disease product application if the rare pediatric disease designation was granted by December 20, 2024, and the BLA or NDA for that product is approved before September 30, 2026. Since we did not receive a rare pediatric disease designation for any candidate product by December 20, 2024, we will not qualify for a PRV unless the Rare Pediatric Disease PRV program is further extended by Congressional action. Further, even if Congress reauthorizes this program and our product candidates are designated as drugs for a rare pediatric disease in a timely manner, we would still not qualify for a PRV unless we secure approval of the BLA or NDA for the product before the date established for such approval in any new legislation reauthorizing this PRV program. Since a PRV may be sold for substantial amounts of money, or used by us to expedite approval of another marketing application, our business may be harmed if we do not qualify for a PRV in connection with approval of an NDA or BLA.

We and our contract manufacturers are subject to significant regulation. The manufacturing facilities on which we rely may not continue to meet regulatory requirements, which could materially harm our business.

All entities involved in the preparation of product candidates, including drug substance, drug product and device combinations that may be used in combination with our product candidates, for clinical trials or commercial sale, including any contract manufacturers, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMPs. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing.

We or our contract manufacturers must supply all necessary documentation in support of a BLA or NDA on a timely basis and must adhere to the FDA's current good laboratory practices and cGMP regulations enforced through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our contract manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of any product candidate. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our contract manufacturers. If any such inspection or audit identifies failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility, which may lead to temporary or permanent supply shortages. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product, or revocation of a pre-existing approval. Any such consequence would severely harm our business, financial condition and results of operations.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, competing priorities or other disruptions to these agencies' operations, and regulatory reform efforts, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the FDA have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies, including government agencies and regulatory authorities outside the United States, on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Further, while the FDA's review of NDAs and BLAs is funded by the user fee program established under PDUFA, the Trump Administration has indicated that it will be reviewing that program and its implementation.

In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the U.S. facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

Disruptions or competing priorities at the FDA and other agencies may also slow the time necessary for new product candidates 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 and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Further, there is substantial uncertainty as to how measures being implemented by the new Trump Administration across the government will impact the FDA, CMS and other federal agencies with jurisdiction over our activities. For example, since taking office, President Trump has issued a number of executive orders, which could have a significant impact on the manner in which the FDA conducts its operations and engages in regulatory and oversight activities. These include E.O. 14192, "Unleashing Prosperity Through Deregulation," issued January 31, 2025; E.O. 14212, "Establishing the President's Make America Healthy Again Commission," issued February 13, 2025; and E.O. 14219, "Ensuring Lawful Governance and Implementing the President's 'Department of Government Efficiency' Deregulatory Initiative," issued February 21, 2025. If these or other orders or executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, with job cuts at the FDA and the loss of key personnel that have recently taken place, we anticipate further disruptions and potential delays in the FDA's review and oversight of our product candidates. Similarly, efforts by the new administration to substantially reduce or delay research funding by the National Institutes of Health of medical research could have substantial direct or indirect impacts on our research activities.

If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Current and future legislation may increase the difficulty and cost for us to obtain reimbursement for any of our product candidates that do receive marketing approval.

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

criteria and in additional downward pressure on the price that we may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain marketing approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, in December 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. In June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA.

Litigation and legislation over the ACA and other healthcare measures are likely to continue, with unpredictable and uncertain results. During the first Trump Administration, Congress and the administration sought to overturn the ACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous executive orders issued by President Biden, including at least two executive orders (e.g., Executive Order 14009, Strengthening Medicaid and the Affordable Care Act, and Executive Order 14070, Continuing to Strengthen Americans' Access to Affordable, Quality Health Coverage) which were designed to further implement the ACA. We anticipate similar efforts to undermine the ACA, and the accompanying uncertainty, for the foreseeable future.

In the European Union, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among European Union Member States in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the European Union level for joint clinical assessments in these areas. It will permit European Union Member States to use common HTA tools, methodologies and procedures across the European Union, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual European Union Member States will continue to be responsible for assessing non-clinical (e.g., economic, social and ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact

the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed.

The prices of prescription pharmaceuticals have been the subject of considerable discussion in the United States. There have been several Congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. With the revocation of executive orders issued by President Biden, there is considerable uncertainty as to how the new administration will continue these efforts. For example, upon taking office, President Trump revoked an executive order that had directed the Center for Medicare and Medicaid Innovation to develop three experimental drug pricing models, leaving their future unclear.

With respect to existing regulatory mechanisms to address the costs of prescription pharmaceuticals, the Department of Health and Human Services, or HHS, and the FDA published a final rule in October 2020 allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of drugs from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of October 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted Section 804 Importation Program proposals to the FDA. Vermont has submitted a concept letter to the HHS. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

In August 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The IRA has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap and it replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025) that would require manufacturers to cover a portion of these costs. In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, the HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, shortly before the new administration took office, CMS announced its selection of 15 additional drugs covered by

Part D for the second cycle of negotiations. There has been uncertainty about the extent to which the new administration would support the price negotiation program. Following the change in administrations, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

In addition, we will need to carefully navigate the IRA and its provisions governing orphan drugs. Specifically, the IRA includes a provision, known as the orphan drug exclusion, that excludes from price negotiations those orphan drugs that have been designated for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Thus, as CMS stated in final guidance in July 2023, a drug or biologic that is designated for more than one rare disease or condition will not qualify for the orphan drug exclusion, even if the drug or biologic is not approved for any indications for the additional diseases or conditions. While there is Congressional support for expanding the orphan drug exclusion to include orphan drugs with more than one approved indication, no legislation has been enacted. Accordingly, if one of our product candidates is designated and approved as an orphan drug for one disease or condition, and we subsequently receive approval of that product for a different disease or condition, the product will no longer be excluded from the IRA price negotiation provision under the orphan drug exclusion and that could impact our revenues and business.

Further, the IRA subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the IRA by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The IRA also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The IRA also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, price caps on annual out-of-pocket expenses, and the requirement that manufacturers cover a portion of these costs, each of which could have potential pricing and reporting implications.

In June 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. There have been various decisions by the courts considering these cases since they were filed. The HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

In addition, at the federal level in the United States, in February 2023, CMS announced a model that would allow CMS to pay less for drugs and biologics approved through FDA's accelerated approval pathway before a clinical benefit has been confirmed by the required confirmatory studies. If implemented, this would impact the price that CMS would pay for Medicare Part B drugs and biologics that fit within CMS's criteria for lower payments. Implementation of this model could result in reduced reimbursement for our products and also lead to further and more expansive pricing pressure from CMS and other U.S. payors, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive 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. This is increasingly true with respect to products approved pursuant to the accelerated approval

pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. In addition, regional healthcare organizations 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. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

The insurance coverage and reimbursement status of newly approved products is uncertain. Our product candidates, if approved, may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain coverage and adequate reimbursement for any of our product candidates for which we obtain approval could limit our ability to market those products and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs and other medical products vary widely from country to country. In the United States, healthcare reform legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more products or product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize our products and product candidates also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Sales of any product we successfully develop will depend substantially, both domestically and abroad, on the extent to which the costs of such product will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels or only after clearing significant barriers, such as the requirement to fail on other products before providing reimbursement, we may not be able to successfully commercialize any product we may successfully develop. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for any product we may successfully develop. Accordingly, in markets outside the United States, the reimbursement for products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payer to payer. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of any product we may successfully develop to each payer separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

In the EU, pricing and reimbursement schemes vary widely from country to country and may be more conservative than CMS. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors any product we may successfully develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates and our overall financial condition.

Further, some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Finally, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates from third-party payors for any product we may successfully develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Increasingly, third-party payors are requiring that pharmaceutical companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers and third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Potentially applicable United States federal and state healthcare laws and regulations include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation.

False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or qui tam actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

False Statements Statute. The federal false statements statute prohibits 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.

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the HHS information related to physician and healthcare provider payments and other transfers of value and physician ownership and investment interests.

Analogous State and Foreign Laws. Analogous state laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations 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 these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, corporate integrity or other similar forms of agreements or decrees, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States, European Union and the United Kingdom. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information that may impact certain of our business operations. For example, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical, and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity, and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In recent months, the Officer of Civil Rights, or OCR, has been especially active in enforcing the HIPAA rules. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. Additionally, OCR is looking to amend the HIPAA Security Rule, which (if and when finalized) could create additional compliance obligations and risk for our business.

In addition to potential enforcement by the HHS, we could also be potentially subject to privacy enforcement from the Federal Trade Commission, or the FTC. The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate risk for a potential enforcement action, which may be costly. Finally, both the FTC and HHS's enforcement priorities (as well as those of other federal regulators) may be impacted by the change in administration and new leadership. These shifts in enforcement priorities may also impact our business.

There are also increased restrictions at the federal level relating to transferring sensitive data outside of the U.S. to certain foreign countries. For example, in 2024, Congress passed H.B. 815, which included the Protecting Americans' Data from Foreign Adversaries

Act of 2024. This law creates certain restrictions for entities that disclose sensitive data (including potential health data) to countries such as China. Failure to comply with these rules can lead to a potential FTC enforcement action. Additionally, the Department of Justice recently finalized a rule implementing Executive Order 14117, which creates similar restrictions related to the transfer of sensitive US data to countries such as China. These data transfer restrictions (and others that may pass in the future) may create operational challenges and legal risks for our business.

There are other privacy and security laws that also may be applicable to our business activities now or in the future. For example, on January 1, 2020, the California Consumer Privacy Act, or CCPA took effect and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the European Union's General Data Protection Regulation, or GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of the "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. The California Privacy Rights Act, or CPRA, went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created an enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA and other California privacy laws, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, at least eighteen other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect over the next few years. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond, including New Hampshire and New Jersey. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that regulates the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2025. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

Similar to the laws in the United States, there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

The GDPR places restrictions on the cross-border transfer of personal data from the European Union to countries that have not been found by the European Commission to offer adequate data protection legislation, such as the United States. There are ongoing concerns about the ability of companies to transfer personal data from the European Union to other countries. In July 2020 the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of

personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. While we were not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the United States generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

In October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which serves as a replacement to the EU-U.S. Privacy Shield. The EC adopted the adequacy decision on July 10, 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge", which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the U.S.

Switzerland has also approved an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which functions similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the U.S.). Any changes or updates to these developments have the potential to impact our business.

Following the withdrawal of the UK from the European Union, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the European Union have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge", which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the United States. In addition to the UK, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, if approved, through increased compliance costs, costs associated with contracting, and potential enforcement actions.

Data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

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

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

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage and other collateral consequences. If any subpoenas, investigations or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Further, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States and the U.K. Bribery Act 2010. Violations of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could significantly harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. For example, on January 20, 2025, European Union regulatory authorities announced that the European Commission is planning to ban per- and polyfluoroalkyl substances, or PFAS, in consumer products, with exemptions for certain essential industrial uses. PFAS, which are also known as "forever chemicals" because they do not break down easily in the environment, have been linked

to serious health problems. This regulatory action, and potentially similar actions in the United States and other jurisdictions could affect the use of certain chemicals that we use in our manufacturing activities. While it is not at all clear whether these regulatory actions will require us to adopt alternatives for such chemicals, such action could impact our plans and anticipated costs for development and approval of our current and any future programs and thereby affect our business. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Our employees, independent contractors, CROs, consultants, contract manufacturers, commercial partners, vendors and principal investigators may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, CROs, consultants, contract manufacturers, commercial partners, vendors and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Even with appropriate policies and procedures, it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Risks Related to Taxation

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us and our stockholders. Many such changes have been made and changes are likely to continue to occur in the future. For example, the TCJA was enacted in 2017 and significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, a limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), a limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and an elimination of net operating loss carrybacks (though any net operating losses generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely), and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. The IRA was also signed into law in August 2022. The IRA introduced new tax provisions, including a one percent excise tax imposed on certain stock repurchases by publicly traded companies. The one percent excise tax generally applies to any acquisition of stock by the publicly traded company (or certain of its affiliates) from a stockholder of the company in exchange for money or other property (other than stock of the company itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. In addition, certain tax laws that are specific to the biopharmaceutical industry, such as the orphan drug tax credit, which was enacted as part of the Orphan Drug Act, have been limited over time and continuing limitations or restrictions of the tax credit and changes to other tax laws applicable to our business could negatively impact our business and results of operations. Additional tax legislation may also be enacted, and regulatory guidance under the TCJA continues

to be forthcoming. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

Our ability to use net operating losses and research and development credits to offset future taxable income may be subject to certain limitations.

In general, under Sections 382 and 383 of the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Under Section 382, the annual limitation is determined by first multiplying the value of the corporation's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required.

As a result of, among other transactions, the shares issued in January 2021 related to the acquisition of Quellis and the February 2021 Financing, we believe we have experienced several historical ownership changes, as defined by Section 382. As a result, our utilization of the federal and state net operating loss carryforwards or research and development tax credit carryforwards are subject to annual limitation under Sections 382 and 383. Our analysis of Section 382 indicates that a significant portion of our Federal and state net operating loss carryforwards and research and development tax credit carryforwards are limited, such that a significant portion of them are anticipated to not be available or expire before utilization.

Risks Related to Employee Matters, Managing Growth and Information Technology

Our future success depends on our ability to retain our senior management and key employees.

We are highly dependent on our executive officers and key employees. If we are unable to retain our executive officers or other key employees, replacing them may be difficult and costly, and may take an extended period of time because of the nature of our current business strategy and the limited number of individuals in our industry with the relevant breadth of skills and experience. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate replacements for our executive officers or key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel.

We rely on consultants and advisors, including financial, legal, scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us.

We may experience difficulty in locating, attracting and retaining experienced and qualified personnel, which could adversely affect our business.

We will need to attract, retain and motivate experienced clinical development and other personnel, particularly in the greater Boston area, as we expand our clinical development activities and prepare for potential commercialization of our product candidates. Personnel with the required skills and experience may be scarce or may not be available at all in this geographic region. In addition, competition for these skilled personnel is intense and recruiting and retaining skilled employees is difficult, particularly for a development-stage company such as ours. If we are unable to attract and retain qualified personnel, our clinical development activities and preparation for potential commercialization of our product candidates may be adversely affected. Even if we are successful in identifying and attracting qualified employees, recent market changes, including labor shortages, and rising inflation have increased employee-related costs substantially, which may negatively affect our operating results.

Security breaches and other disruptions to our information technology systems could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, as well as our proprietary business information, employee data and personally identifiable information of clinical trial participants in accordance with

informed consents covering such information as well as personal information of other individuals. We also rely to a large extent on computer and information technology systems to operate our business. Remote working arrangements could impact employees' productivity and morale, strain our technology resources and introduce operational risks. Additionally, the risk of cyber-attacks or other privacy or data security incidents may be heightened as a result of our hybrid working environment, the remote working aspects of which may be less secure and more susceptible to hacking attacks. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. The secure maintenance of this information is important to our operations and business strategy. Despite our security measures, our information technology infrastructure, and that of our vendors and third-party providers, may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our vendors and third-party providers could be susceptible to third party attacks on our and their information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. The risk of a security breach or disruption through cyber-attacks has generally increased as the number, intensity and sophistication of attempted attacks from around the world have increased. If a ransomware attack or other cybersecurity incident occurs, either internally or at our vendors or third-party technology service providers, we could be prevented from accessing our data or systems, which may cause interruptions or delays in our business operations, cause us to incur remediation costs, subject us to demands to pay a ransom, or damage our reputation, regardless of whether we pay the ransom amount. While we continue to build and improve our information technology security systems and infrastructure, there can be no assurance that our efforts will prevent service interruptions, breakdowns or security breaches. For example, we have detected common types of attempts to attack our information technology systems and data using means that have included phishing. Any service interruptions or security breaches of our information technology systems may substantially impair our ability to operate our business and could compromise our networks, or those of our vendors and third-party providers, and the information stored could be accessed, publicly disclosed, lost or stolen.

We may be required to expend significant resources (including financial), fundamentally change our business activities and practices, or modify our operations, including our clinical trial activities, or information technology in an effort to protect against security breaches and to detect (including performing required forensics), mitigate and remediate actual and potential vulnerabilities. Relevant laws, regulations, industry standards and contractual obligations may require us to implement specific security measures or use industry-standard or reasonable measures to protect against security breaches. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs, security breaches and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, data loss or corruption, delays, cessation of service and other harm to our business and our competitive position. If the information technology systems of our third-party vendors become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business. Although we maintain cyber liability insurance, it may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches.

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information and personal data.

Issues in the use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. Our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If any of our vendors experiences an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

Risks Related to Our Common Stock

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

Our holders of 5% or more of our capital stock and their respective affiliates beneficially own in excess of 67% of our outstanding common stock. These stockholders, acting together or on their own, may be able to impact matters requiring stockholder approval. For example, they may be able to impact elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that investors may feel are in their best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with each investor's interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

The price of our common stock has been and is likely to continue to be highly volatile, which could result in substantial losses for our stockholders.

Our stock price has been and is likely to continue to be highly volatile. For example, when we announced our acquisition of Quellis, our stock price increased by approximately 70% in one day. In the twelve months ending February 28, 2025, the last business day in February, our stock price has traded at a high of $16.90 and a low of $6.20.

The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our investors may lose some or all of their investments. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of navenibart, STAR-0310 or any future product candidate;
- commencement or termination of collaborations for any development programs we may pursue;
- failure or discontinuation of any of any development programs we may pursue;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to a product candidate or clinical development program;
- the results of any additional efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or recommendations by securities analysts that cover our stock;
- announcement or expectation of additional financing efforts;
- announcement of collaborations, licenses, acquisitions or other comparable forms of transactions;
- sales of our common stock by us, our insiders or other stockholders;

- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including political instability, war or instability from public health crises, pandemics or epidemics; and
- the other factors described in this "Risk Factors" section.

Additionally, securities class action litigation has often been brought against a company following a decline in the market price of its securities. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

As a public company we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including those related to climate change and other environmental, social and governance focused disclosures, are creating uncertainty for public companies, increasing legal and financial compliance costs, and making some activities more time consuming. Our management and other personnel devote a substantial amount of time towards maintaining compliance with the corporate governance and public disclosure rules and regulations that are applicable to us and will continue to do so. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. In addition, if we cease to be a smaller reporting company, we will need to comply with significant additional disclosure and other obligations.

Pursuant to Section 404 of SOX, we are required to furnish reports by our management on our internal control over financial reporting with our Annual Reports on Form 10-K with the SEC. If we cease to be a smaller reporting company with less than $100 million in annual revenue, we will also be required to include attestation reports on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404 of SOX. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of February 28, 2025, we had outstanding 56,434,219 shares of common stock and 31,107 shares of Series X Preferred Stock, which are convertible into 5,184,591 shares of common stock. We have registered under the Securities Act of 1933, as amended, or the Securities Act, 15,399,967 shares of our common stock issued to the former Quellis stockholders or issued or issuable upon conversion of the Series X Preferred Stock. As a result, such shares are freely tradable without restriction under the

Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any significant sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity offerings. In addition, in connection with any merger, consolidation or sale of all or substantially all of our assets, holders of our outstanding warrants would be entitled to receive consideration in excess of their reported beneficial ownership of our common stock and this could adversely impact the consideration our other stockholders would receive.

As part of our registered offering of common stock in October 2023, we issued common stock warrants to purchase an aggregate of 7,368,738 shares of our common stock, and pre-funded warrants to purchase up to an aggregate of 1,571,093 shares of our common stock. Each pre-funded warrant has an exercise price per share of common stock equal to $0.001 per share. Each pre-funded warrant is exercisable from the date of issuance until exercised in full solely by means of a cashless exercise. Each common stock warrant has an exercise price per share of common stock equal to $8.025. Each common stock warrant is exercisable from the date of issuance until October 16, 2028. Each common stock warrant is exercisable solely by means of a cash exercise, except that the common stock warrant is exercisable via cashless exercise if at the time of exercise, a registration statement registering the issuance of the shares of common stock underlying the common stock warrants under the Securities Act is not then effective. The common stock warrants include certain rights upon "fundamental transactions" as described in the common stock warrants, including the right of the holders thereof to receive from us or a successor entity the same type or form of consideration (and in the same proportion) that is being offered and paid to the holders of common stock in such fundamental transaction in the amount of the Black Scholes value (as described in such common stock warrants) of the unexercised portion of the applicable common stock warrants on the date of the consummation of such fundamental transaction. A holder of common stock warrants (together with its affiliates) may not exercise any portion of a common stock warrant to the extent that the holder would beneficially own more than 4.99% (or, at the election of the holder, 9.99%) of our outstanding common stock immediately after exercise.

Although these warrants issued in October 2023 are subject to beneficial ownership limitations, upon exercise in full of the warrants, the shares issuable upon exercise would represent a significant portion of our outstanding common stock. As a result, the holders of these warrants may be able to exert substantial influence over our business. The concentration of voting power resulting from the exercise of the warrants could delay, defer or prevent a change of control, entrench our management and our board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and the holders of these warrants, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters. In addition, sales of these shares could cause the market price of our common stock to decline significantly.

We have registered the issuance of shares upon exercise of these warrants under registration statements. As a result, the shares issuable upon exercise of these warrants can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. Sales of these shares could cause the market price of our common stock to decline significantly. Furthermore, if our stock price rises, the holders of these warrants may be more likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our common stock and reduce or eliminate any appreciation in our stock price that might otherwise occur.

Given the amount and terms of these warrants, we may find it more difficult to raise additional equity capital on favorable terms or at all while these warrants are outstanding.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future, accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. Any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be investors' sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock will likely depend, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

Risks Relating to our Certificate of Incorporation and Bylaws

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our investors might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

In addition, as of February 28, 2025, there are 31,107 shares of our Series X Preferred Stock outstanding that we issued in connection with the acquisition of Quellis and the February 2021 Financing. Except as otherwise required by law, the Series X Preferred Stock does not have voting rights. However, as long as any shares of Series X Preferred Stock are outstanding, we may not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series X Preferred Stock, (i) alter or change adversely the powers, preferences or rights given to the Series X Preferred Stock or alter or amend the Certificate of Designation that authorized the Series X Preferred Stock, amend or repeal any provision of, or add any provision to, our Certificate of Incorporation or bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series X Preferred Stock, (ii) issue further shares of Series X Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series X Preferred Stock, or (iii) enter into any agreement with respect to any of the foregoing.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Our certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors and officers.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, or any action asserting a claim against us governed by the internal affairs doctrine. These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers, or employees, which may discourage such lawsuits against us and our directors, officers, and employees. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition, and operating results. This exclusive forum provision would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, which provides for exclusive jurisdiction of the federal courts. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder; provided, that with respect to claims under the Securities Act, our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Cybersecurity Risk Management and Strategy

We have established processes to assess, identify, and manage cybersecurity risks. These processes are integrated into our overall risk management program and are designed to protect our information assets from internal and external cyber threats and include:

- implementing physical, procedural, and technical safeguards;
- developing and maintaining comprehensive response plans;
- conducting regular exercises and tests to identify potential vulnerabilities;
- engaging with external cybersecurity experts to enhance our oversight and keep pace with evolving threats; and
- considering the cybersecurity capabilities of partners and third-party service providers, both prior to engaging them and on an ongoing basis.

Cybersecurity Governance and Oversight

Our board of directors provides direct oversight of cybersecurity risk and has delegated to its audit committee the responsibility of reviewing and discussing with management our risk exposures relating to cybersecurity. The board of directors and the audit committee conduct periodic reviews of our cybersecurity readiness to ensure continuous improvement in our cybersecurity strategies and receive regular updates from management on cybersecurity matters and are promptly informed by management about any significant new threats or incidents.

We have implemented robust mechanisms to monitor and manage cybersecurity threats and incidents, including utilization of advanced tools for continuous monitoring of our IT environment to detect and mitigate threats, a fundamental plan for responding to cyber incidents and training for employees to recognize and report potential cybersecurity incidents and to foster a culture of cybersecurity awareness and vigilance. We have a dedicated management team, led by our Vice President of IT, that is responsible for operational oversight of our cybersecurity strategy and policies. Our Vice President of IT has an extensive background in IT management with a focus on securing sensitive biotech data and systems, having held similar roles at two previous biotech companies with responsibilities including corporate infrastructure and cyber security readiness and response, in addition to over 20 years of professional experience in IT. Any identified cybersecurity incident is reported to our cybersecurity management team, which evaluates the severity of the incident. Based on this assessment, further steps are taken involving other members of management and, depending on the severity, the audit committee and the board of directors. We believe this structured approach allows us to effectively manage and mitigate cybersecurity risks, safeguarding our systems and data against various digital threats. Additionally, our proactive stance is supported by comprehensive cybersecurity insurance, which further reinforces our preparedness against potential cyber threats.

Cybersecurity Incident Reporting and Management

We have not identified any risks from cybersecurity threats that have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition. However, we remain vigilant and prepared to respond effectively to any incidents, should they arise.

Item 2. Properties

Our offices are located in Boston, Massachusetts and consist of approximately 30,110 square feet of subleased office space under a lease that is scheduled to end on November 30, 2028 or on such earlier date as the term may sooner cease or expire as set forth in the sublease agreement. We believe that our existing facilities are sufficient for our needs for the foreseeable future.

Item 3. Legal Proceedings

From time to time we may become subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this Annual Report on Form 10-K, we do not believe we are party to any claim or litigation, the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable

PART II

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

Market Information

On September 9, 2021, following our name change to Astria Therapeutics, Inc., our common stock, $0.001 par value per share, commenced trading under the symbol "ATXS" on the Nasdaq Global Select Market. Prior to September 9, 2021, our common stock was publicly traded on the Nasdaq Global Market under the symbol "CATB" since June 25, 2015. Prior to that time, there was no public market for our common stock.

Holders

As of February 28, 2025, there were approximately 19 holders of record of our common stock. This number of holders of record does not include beneficial owners of our common stock 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.

Dividends

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

Recent Sales of Unregistered Securities

We did not sell or issue any equity securities that were not registered under the Securities Act during the period covered by this Annual Report on Form 10-K.

Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Reserved

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. This section provides additional information regarding our businesses, current developments, results of operations, cash flows, financial condition, contractual commitments and critical accounting policies and estimates that require significant judgement and have the most potential impact on our consolidated financial statements. This discussion and analysis is intended to better allow investors to view the Company from the management's perspective.

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for allergic and immunological diseases. Our focus is to develop first-choice therapies that improve the health and outcomes of patients with allergic and immunologic diseases. Our lead product candidate is navenibart, formerly known as STAR-0215, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in clinical development for the treatment of hereditary angioedema, or HAE, a rare, debilitating and potentially life-threatening disease. We believe that navenibart has the potential to be the market-leading and most patient-friendly chronic treatment option for HAE, based on proof-of-concept data in HAE patients and the existing HAE treatment landscape. Our second product candidate is STAR-0310, a monoclonal antibody OX40 antagonist that is in clinical development for the treatment of atopic dermatitis, or AD, an immune disorder associated with loss of skin barrier function and itching. We believe that with both of these programs, we are advancing a pipeline of products with meaningfully differentiated profiles based on validated mechanisms.

Navenibart

The treatment options for patients with HAE have improved in recent years, however, there is remaining unmet medical need and the global market for HAE therapy is strong and growing. The goal for navenibart is to develop a best-in-class monoclonal antibody inhibitor of plasma kallikrein able to provide long-acting, effective attack prevention for HAE. Our vision for navenibart is to lead the HAE market and become the first-choice preventative treatment for HAE with administration every three and six months with the goal of normalizing the lives of people living with HAE. Targeted plasma kallikrein inhibition can prevent HAE attacks by suppressing the pathway that generates bradykinin and causes excessive swelling. Navenibart is currently in clinical development and the U.S. Food and Drug Administration, or FDA, has granted Fast Track and Orphan Drug designations to navenibart for the treatment of HAE. The European Commission has granted Orphan Medicinal Product Designation to navenibart for the treatment of HAE.

In February 2025, we initiated a Phase 3 trial of navenibart called ALPHA-ORBIT. This global, randomized, double-blind, placebo-controlled trial is evaluating the efficacy and safety of navenibart over a 6-month treatment period in up to 135 adults and 10 adolescents (open-label), with Type 1 or Type 2 HAE. Adult patients will be randomized to receive one of three navenibart dose arms: 1) an initial 600 mg dose followed by 300 mg every 3 months (Q3M), 2) 600 mg every six months (Q6M), 3) 600 mg Q3M, or placebo; adolescents will receive an initial 600 mg dose followed by 300 mg Q3M. The dose arms support the potential to provide patient-centered dosing flexibility to people with HAE. The primary endpoint is time-normalized monthly HAE attacks at 6 months, and a key secondary endpoint includes the proportion of participants who are attack-free at 6 months. After 6 months, patients may be eligible to enter ORBIT-EXPANSE, a long-term trial, in which all patients will be treated with navenibart (open-label) and which will include a patient-centered flexible dosing period. The navenibart Phase 3 program will consist of the ALPHA-ORBIT Phase 3 trial and ORBIT-EXPANSE, which are designed to support registration globally. Top-line results from the ALPHA-ORBIT trial are anticipated in early 2027. In addition, to ease the administration of navenibart, we are developing both autoinjector and pre-filled syringe drug device combinations.

In February 2023, we initiated a Phase 1b/2 trial of navenibart called ALPHA-STAR, or Astria Long-acting Prophylaxis for Hereditary Angioedema: STAR-0215. This global, multi-center, open-label, single and multiple dose proof-of-concept clinical trial in people with HAE evaluated safety, tolerability, HAE attack rate reduction, pharmacokinetics, or PK, pharmacodynamics, or PD, and quality of life in patients three and six months after subcutaneous navenibart administration. We reported initial proof-of-concept data in HAE patients in March 2024. Target enrollment of 16 patients was achieved with all doses administered and we reported final results from ALPHA-STAR target enrollment in December 2024 which were as follows:

Cohort 1 evaluated a single 450 mg dose (n=4). The results for the cohort measured over 6 months were averages of:

- a 91% reduction in monthly attack rate;
- a 96% reduction in moderate and severe attacks; and
- a 94% reduction in acute rescue medication use; with
- 50% of patients being attack-free through 3 months of follow-up, and 25% being attack-free through 6 months of follow-up.

Cohort 2 evaluated a 600 mg dose followed by a 300 mg dose three months later, on Day 84 (n=6). The results for the cohort measured over 6 months were averages of:

- a 95% reduction in monthly attack rate;
- a 95% reduction in moderate and severe attacks; and
- a 94% reduction in acute rescue medication use; with
- 67% of patients being attack-free.

Cohort 3 received a 600 mg dose followed by a 600 mg dose one month later, on Day 28 (n=6). The results for the cohort measured over 6 months were averages of:

- a 92% reduction in monthly attack rate;
- a 96% reduction in moderate and severe attacks; and
- a 91% reduction in acute rescue medication use; with
- 67% of patients being attack-free.

Navenibart was generally well-tolerated with no serious treatment-emergent adverse events, or TEAEs, and no discontinuations. There were four non-severe and quickly resolved treatment-related TEAEs: one case of dizziness, one transient injection site reaction (rash), one case of injection site erythema, and one case of injection site pruritus. There were no injection site reactions of pain.

In October 2024, we presented new quality of life data from initial results from ALPHA-STAR at the American College of Allergy Asthma and Immunology (ACAAI) demonstrating that navenibart induced rapid improvements in quality of life in HAE patients. By day 28 after navenibart administration, 80% of participants achieved clinically meaningful improvements.

Enrollment in ALPHA-STAR was expanded and a total of 29 patients were enrolled in the trial in order to accelerate the collection of data to support potential regulatory filings and future approvals.

ALPHA-SOLAR, a long-term open-label trial assessing the long-term safety and efficacy of navenibart, is ongoing. All of the 29 patients from ALPHA-STAR have entered ALPHA-SOLAR. Participants are being assigned to receive navenibart in one of two dosing regimens: either 300mg Q3M or 600mg Q6M. We expect to report initial safety and efficacy data from ALPHA-SOLAR in mid-2025.

STAR-0310

We believe that OX40 inhibition has the potential to treat AD and other diseases. The current treatment options in AD are insufficient to address the needs of many patients, and standard of care treatments include steroids and topical medications which can treat symptoms but do not address the underlying disease. Our goal for STAR-0310 is to reduce disease activity, relapse rate, and treatment burden for patients with moderate-to-severe AD. STAR-0310 was engineered with YTE half-life extension technology to enable infrequent dosing. As a potential long-acting OX40 inhibitor, STAR-0310 aims to address the need for a safe, effective, and infrequently administered AD treatment.

In January 2025, we announced the initiation of our Phase 1a trial of STAR-0310 in healthy subjects. The Phase 1a randomized, double-blind, placebo-controlled single ascending dose trial is evaluating the safety, tolerability, PK, and immunogenicity of STAR-0310 in approximately 40 healthy adult participants. We anticipate early proof-of-concept results from the trial in the third quarter of 2025.

In May 2024, we shared preclinical results for STAR-0310 at the European Academy of Allergy and Clinical Immunology (EAACI) conference. STAR-0310 exhibited a long mean half-life of 26 days in cynomolgus monkeys compared to a half-life of 10-14 days for a typical non-half-life - extended IgG antibody. There was also an approximately 8-fold increase in binding affinity to human OX40 observed for STAR-0310 compared to telazorlimab, an earlier generation antibody prior to affinity maturation without half-life extension. Preclinical results demonstrated significantly less antibody-dependent cellular cytotoxicity, or ADCC, potential with STAR-0310 compared to rocatinlimab, an anti-OX40 monoclonal antibody in Phase 3 development by Amgen, Inc., with comparable potency. Having less ADCC in the context of robust potency could potentially result in a favorable safety profile and potentially wider therapeutic window for STAR-0310. We believe these preclinical results support the potential for STAR-0310 to have the best-in-class OX40 inhibitor profile.

Assuming positive results from the Phase 1a clinical trial, we are planning a proof-of-concept clinical trial of STAR-0310 in patients with AD. The goals of the proof-of-concept trial would be to demonstrate initial efficacy in AD as well as show differentiation in safety and tolerability and the potential for a reduced treatment burden as a result of extended half-life as compared to existing therapies.

Financial Overview

Our business is almost entirely dependent on the success of navenibart and STAR-0310. Navenibart is in clinical development and has only produced results in Phase 1a and Phase 1b/2 clinical testing and in preclinical and nonclinical settings. STAR-0310 entered into early clinical development in January 2025. Our net losses were $94.3 million and $72.9 million (including $15.2 million of in-process research and development, or IPR&D, expenses) for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $674.8 million. We have not generated any product revenues and have financed our operations primarily through public offerings and private placements of our equity securities and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical development programs.

As of December 31, 2024, we had $328.1 million in cash, cash equivalents and short-term investments, which we expect will enable us to fund our operating expenses and capital expenditure requirements into mid-2027. Our current operating plan includes the development of navenibart and STAR-0310, including (i) for navenibart, support for all program activities through completion of our ALPHA-ORBIT Phase 3 trial, including activities related to the planned ORBIT-EXPANSE long term trial and Phase 3 development and testing of drug device combinations for potential dosing of navenibart, and (ii) for STAR-0310, the completion of the ongoing Phase 1a clinical trial of healthy subjects and any related anticipated milestone payments. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Advancing the development of navenibart, any drug device combination for navenibart, STAR-0310 or any future product candidates will require a significant amount of capital and our existing cash, cash equivalents and short-term investments will not be sufficient to enable us to fund the completion of development of any of our product candidates, including navenibart, any drug device combination for navenibart, STAR-0310 or any future product candidate. We will need to obtain substantial additional funding to complete the development and commercialization of navenibart, any drug device combination for navenibart, STAR-0310 or any future product candidates and support our continuing operations, future clinical trials and expansion of our pipeline. Furthermore, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional financing to fund our long-term operations sooner than planned. See the section titled “Liquidity and Capital Resources” below for additional information.

Revenue

As of December 31, 2024, we have not generated any revenue from product sales.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates and drug device combination candidates, which include:

- employee-related expenses including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct clinical trials and research and development and preclinical activities on our behalf;
- the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing study and clinical trial materials; and

- facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

We typically use our employee, consultant and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or external consultant costs to specific product candidates or development programs. We record our research and development expenses net of any research and development tax incentives we are entitled to receive from government authorities.

The following table summarizes our research and development expenses by program (in thousands):

	Year Ended December 31,	
	2024	2023
Navenibart	$ 32,401	$ 24,186
STAR-0310	15,497	677
Other programs	811	4,144
Costs not directly allocated to programs:		
Employee expenses including cash compensation, benefits and stock-based compensation	18,196	11,162
Consultants and professional expenses	8,496	1,278
Facilities	801	325
Other	904	355
Total costs not directly allocated to programs	28,397	13,120
Total research and development expenses	$ 77,106	$ 42,127

We expect to incur significant research and development expenses in the year ending December 31, 2025, and in future periods in connection with the clinical trials and other activities related to the development of navenibart and one or more drug device combinations for navenibart, and the preclinical studies, planned clinical trials and other activities related to the development of STAR-0310. Because of this, we expect that our research and development expenses over the next several quarters will be higher than the prior year periods. Development of navenibart, drug device combinations for navenibart, STAR-0310 and any future product candidates is highly uncertain and we cannot reasonably estimate at this time the nature, timing and costs of the efforts that would be necessary to complete the development of any such product candidates. We are also unable to predict when, if ever, material net cash inflows would commence from navenibart, STAR-0310 or any other future product candidates. This is due to the fact that we would need to raise substantial additional capital to fund the completion of the clinical development of any such product candidates and the numerous risks and uncertainties associated with developing and commercializing product candidates, including the uncertainties of:

- establishing an appropriate safety profile with IND-enabling toxicology studies;
- successful design of, enrollment in, and completion of clinical trials;
- feedback from the FDA and foreign regulatory authorities on planned trial designs, preclinical studies and manufacturing capabilities and plans;
- changes in the FDA and foreign regulatory approval processes or perspectives that may delay or prevent the approval of new products;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- launching commercial sales, if we are able to obtain marketing approval, whether alone or in collaboration with others, and our ability to compete successfully with other products; and
- maintaining a continued acceptable safety profile following approval.

A change in the outcome of any of these variables with respect to the development of navenibart, any drug device combination for navenibart, STAR-0310 or any future product candidate, would significantly change the costs and timing associated with the development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, information technology, new product planning, business development, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase from their current levels as we continue to grow our company, develop navenibart, drug device combinations for navenibart, and STAR-0310, and potentially expand our pipeline to include other product candidates.

Acquired In-process Research and Development Expense

Acquired in-process research and development, or IPR&D, expense resulted from our license agreement, or the Ichnos License Agreement, that we entered into with Ichnos Sciences SA and Ichnos Sciences Inc., or collectively Ichnos. In the estimation of fair value of the asset purchase consideration, we primarily used the upfront license fee of $15.0 million as the most reliable indicator of fair value attributable to the acquired IPR&D. As the single identifiable asset, "ISB 830-X8", referred to by us as the STAR-0310 candidate, had not, at the time of the Ichnos License Agreement, received regulatory approval in any territory, the acquisition cost allocated to acquire IPR&D with no alternative future use was recorded as expense at the acquisition date and no additional IPR&D expense relating to the Ichnos License Agreement is expected to be reported in future periods.

Other Income (Expense)

Other income (expense), net consists of interest and investment income earned on our cash, cash equivalents and short-term investments, net of amortization expense on short-term investments, and gains and losses related to foreign currency fluctuations.

Critical Accounting Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be 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.

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

License Agreement

We have concluded that the Ichnos License Agreement was not the acquisition of a business, as substantially all of the fair value of the gross assets acquired was concentrated in the STAR-0310 candidate. STAR-0310 is STAR-0310 candidate engineered with YTE half-life extension technology.

We determined that the cost to acquire the licensed intellectual property assets was $15.2 million, primarily based on the fair value of the upfront license fee of $15.0 million attributable to the acquired IPR&D. As the STAR-0310 candidate had not, at the time of the Ichnos License Agreement, received regulatory approval in any territory, the cost attributable to the IPR&D was expensed in our consolidated statements of operations and comprehensive loss for the year ended December 31, 2023 as the acquired IPR&D had no alternative future use, as determined by us in accordance with U.S. GAAP.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The estimate of accrued research and development expense is dependent, in part, upon the receipt of timely and accurate reporting from CROs and other third-party service providers. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by CROs in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to contracts with CROs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs will exceed the level of services provided and result in a prepayment of the research and development expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting expense amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023, together with the dollar change in those items (in thousands):

	Year Ended December 31,		Period-to-Period Change
	2024	2023	
Operating expenses:			
Research and development	$ 77,106	$ 42,127	$ 34,979
General and administrative	34,452	25,704	8,748
Acquired in-process research and development	—	15,199	(15,199)
Total operating expenses	111,558	83,030	28,528
Loss from operations	(111,558)	(83,030)	(28,528)
Other income, net	17,298	10,139	7,159
Net loss	$ (94,260)	$ (72,891)	$ (21,369)

Research and Development Expenses

Research and development expenses (excluding acquired IPR&D from the Ichnos License Agreement) increased by $35.0 million to $77.1 million for the year ended December 31, 2024 from $42.1 million for the year ended December 31, 2023, an increase of 83%. The increase in research and development expenses was associated with the STAR-0310 program's manufacturing and IND-enabling activities, external research and development costs associated with the navenibart program's advancement in our multi-site international clinical trials and start-up activities to support the ALPHA-ORBIT Phase 3 trial. These research and development activities resulted in a $14.8 million increase in expenses related to external research, manufacturing, and IND-enabling activities related to the STAR-0310 program, a $8.2 million increase in CRO and manufacturing expenses to support the ALPHA-STAR and ALPHA-SOLAR clinical trials in addition to start-up activities to support ALPHA-ORBIT, a $7.2 million increase in consulting expenses primarily to support initial start-up of ALPHA-ORBIT, a $7.0 million increase in employee expenses partially due to a $2.5 million increase in employee stock-based compensation expenses and additional costs related to company growth, and a $1.1 million increase in facilities and other costs, partially offset by a $3.3 million decrease in expenses attributable to other research programs.

General and Administrative Expenses

General and administrative expenses increased by $8.8 million to $34.5 million for the year ended December 31, 2024 from $25.7 million for the year ended December 31, 2023, an increase of 34%. The increase in general and administrative expenses was attributable to a $6.5 million increase in employee expenses primarily due to a $4.1 million increase in employee stock-based compensation expenses and additional costs related to company growth, a $2.0 million increase in professional services due to increased legal fees and consulting expenses, and a $0.3 million increase in other costs, including general office, facilities, and insurance expenses.

Acquired In-Process Research and Development

Acquired IPR&D expense was $15.2 million during the year ended December 31, 2023. Acquired IPR&D expense resulted from the Ichnos License Agreement. The upfront costs of the Ichnos License Agreement and external legal fees attributable to the Ichnos License Agreement were allocated to acquired IPR&D with no alternative future use and were recorded as an expense as of the date of the Ichnos License Agreement. No acquired IPR&D expenses were incurred during the year ended December 31, 2024.

Other Income, Net

Other income, net increased by $7.2 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The increase was primarily attributable to an increase in interest and investment income due to an increase in interest-earning assets from financing proceeds.

Liquidity and Capital Resources

From our inception through December 31, 2024, we raised an aggregate of $839.2 million through equity financings including private placements of preferred stock before we became a public company, our private placement of preferred stock in February 2021 and registered offerings of our common stock, including our at-the-market offering programs.

As of December 31, 2024, we had $328.1 million in cash, cash equivalents and short-term investments, which we expect will enable us to fund our operating expenses and capital expenditure requirements into mid-2027. Our current operating plan includes the development of navenibart and STAR-0310, including (i) for navenibart, support for all program activities through completion of our ALPHA-ORBIT Phase 3 trial, including activities related to the planned ORBIT-EXPANSE long term trial and Phase 3 development and testing of drug device combinations for potential dosing of navenibart, and (ii) for STAR-0310, the completion of the ongoing Phase 1a clinical trial of healthy subjects and any related anticipated milestone payments. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Furthermore, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional financing to fund our long-term operations sooner than planned.

Advancing the development of navenibart, drug device combinations for navenibart, STAR-0310, or any future product candidates will require a significant amount of capital and our existing cash, cash equivalents and short-term investments will not be sufficient to enable us to fund the completion of development of any of our product candidates, including navenibart, drug device combinations for navenibart, STAR-0310 or any future product candidate. In addition, navenibart, STAR-0310, or any future product candidates, if

approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates that we do not expect to be commercially available for years, if at all. Accordingly, we will need to obtain substantial additional funding to complete the development and commercialization of navenibart, drug device combinations for navenibart, STAR-0310 or any future product candidates, support our continuing operations, future clinical trials and the expansion of our pipeline. Adequate additional financing may not be available to us on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of our stockholders. General economic conditions, both inside and outside the United States, including heightened inflation, capital market instability and volatility, interest rate and currency rate fluctuations and economic slowdown or recession as well as pandemics, epidemics and geopolitical events, including civil or political unrest (such as the Ukraine-Russian war and the conflict in the Middle East), may have a significant impact on the availability of funding sources and the terms on which any funding may be available. In addition, market instability and volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity. If we fail to raise capital as, and when, needed, we may be unable to continue our operations at planned levels and be forced to modify our business strategies and reduce or terminate our operations. Although we will continue to pursue these plans, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations when needed or at all.

October 2023 Financing

On October 16, 2023, we closed an underwritten offering of (i) 8,253,895 shares of our common stock and accompanying common stock warrants to purchase an aggregate of 6,190,418 shares of common stock and (ii), in lieu of common stock to certain investors, pre-funded warrants to purchase up to an aggregate of 1,571,093 shares of common stock and accompanying common stock warrants to purchase up to an aggregate of 1,178,320 shares of common stock, which we refer to as the October 2023 Financing. The gross proceeds of the October 2023 Financing were $64.0 million and net proceeds were $59.5 million.

February 2024 Financing

On February 1, 2024, we closed an underwritten offering of 10,340,000 shares of our common stock, which we refer to as the February 2024 Financing. The gross proceeds of the February 2024 Financing were $125.0 million and net proceeds were $117.2 million.

At-the-Market Offerings

In June 2021, we entered into an Open Market Sale Agreement℠ with Jefferies LLC, or Jefferies, pursuant to which we could issue and sell shares of common stock under an at-the-market offering program, or the 2021 ATM Program, which was completed in the first quarter of 2024. In March 2024, we entered into a new Open Market Sale Agreement℠ with Jefferies, pursuant to which we are able to issue and sell up to $150.0 million of shares of common stock under an at-the-market offering program, which we refer to as the 2024 ATM Program and, collectively with the 2021 ATM Program, as the ATM Programs. We pay Jefferies commissions of up to 3% of the gross proceeds from any common stock sold through the ATM Programs. During the year ended December 31, 2024, we sold an aggregate of 4,450,425 shares of common stock under the ATM Programs for gross proceeds of $36.2 million and net proceeds of $35.2 million. During the year ended December 31, 2023, we sold an aggregate of 4,738,606 shares of common stock under the 2021 ATM Program for gross proceeds of $29.4 million and net proceeds of $28.5 million.

Funding Requirements

Our primary uses of capital are for compensation and related expenses, manufacturing costs for preclinical and clinical materials, third party preclinical and clinical research and development services, clinical costs, legal and other regulatory expenses and general overhead.

As of December 31, 2024, we had an accumulated deficit of $674.8 million. We have been primarily involved with research and development activities and have incurred operating losses and negative cash flows from operations since our inception.

Based on our current operating plan, we expect that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into mid-2027. Our current operating plan includes the development of navenibart and STAR-0310, including (i) for navenibart, support for all program activities through completion of our ALPHA-ORBIT Phase 3 trial, including activities related to the planned ORBIT-EXPANSE long term trial and Phase 3 development and testing of drug device combinations for potential dosing of navenibart, and (ii) for STAR-0310, the completion of the ongoing Phase 1a clinical trial of healthy subjects and any related anticipated milestone payments. Our estimate as to how long we expect our cash, cash equivalents and

short-term investments to be able to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of biotechnology products, we are unable to estimate the exact amount of our operating capital requirements. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including:

- the progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for navenibart, any drug device combination for navenibart, STAR-0310, and any future product candidates, including potential future clinical trials;
- our ability to enter into and the terms and timing of any collaborations, licensing or other arrangements that we may establish;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, market access, distribution, supply chain and manufacturing capabilities, and scaling up the manufacturing of drug substance and drug product to clinical and commercial scale and developing a drug device combination, if applicable, securing all raw materials necessary to conduct such scale-up and successfully completing all other activities related thereto;
- if we obtain marketing approval of any of our product candidates, revenue, if any, received from commercial sales of our product candidates;
- if we obtain marketing approval of any of our product candidates, our ability to successfully compete against other approved products that are approved or used as treatments for the indications for which our products are approved, including with respect to navenibart in HAE and STAR-0310 in AD;
- our headcount growth and associated costs;
- the amount and timing of future milestone and royalty payments potentially payable to Ichnos pursuant to the Ichnos License Agreement covering STAR-0310 and our research services agreement related to navenibart;
- The costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, navenibart, including any drug device combination for navenibart, STAR-0310 or any future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing, if available, would result in periodic payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

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

Cash Flows

Comparison of the Years Ended December 31, 2024 and 2023

The following table provides information regarding our cash flows for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Net cash used in operating activities	$ (81,212)	$ (68,445)
Net cash (used in) provided by investing activities	(191,863)	135,052
Net cash provided by financing activities	157,202	88,398
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (115,873)	$ 155,005

Net Cash Used in Operating Activities

Net cash used in operating activities was $81.2 million for the year ended December 31, 2024 and consisted primarily of a net loss of $94.3 million partially offset by $8.5 million of total net non-cash items in addition to a $4.6 million net decrease in other assets. Total net non-cash items consisted primarily of stock-based compensation expense of $13.0 million, a decrease to our right of use asset of $1.0 million, and a $0.1 million decrease in other non-cash items, partially offset by accretion of the discount/premium on investment securities of $5.6 million. The net decrease in other assets consisted of an increase in accrued expenses of $3.7 million and an increase in accounts payable of $2.8 million, which were partially offset by an increase in prepaid expenses and other assets of $1.2 million and a decrease in lease liability of $0.7 million.

Net cash used in operating activities was $68.4 million for the year ended December 31, 2023 and consisted primarily of a net loss of $72.9 million adjusted for stock-based compensation expense of $6.3 million, an adjustment to our right of use asset of $0.6 million, and a net increase in net assets of $2.4 million, which resulted primarily from an increase in prepaid expenses and long term deposits of $4.5 million and a decrease in the lease liability of $0.6 million, partially offset by an increase in accrued expenses of $2.0 million, and an increase in accounts payable of $0.7 million.

Net Cash Provided by (Used in) Investing Activities

Net cash used in investing activities was $191.9 million for the year ended December 31, 2024 and consisted primarily of purchases of short-term investments of $4.2 billion, partially offset by maturities of short-term investments of $4.0 billion as the proceeds from maturities of short-term investments, primarily repurchase agreements with short-term maturities due, purchased and reinvested during the year ended December 31, 2024. Refer to Note 4, “Short-Term Investments” to our consolidated financial statements included in this Annual Report on Form 10-K for additional information.

Net cash provided by investing activities was $135.1 million for the year ended December 31, 2023 and primarily consisted of proceeds from maturities of short-term investments of $2.1 billion, partially offset by purchases of short-term investments of $1.9 billion.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $157.2 million during the year ended December 31, 2024, which was attributable to net proceeds of $117.2 million from the February 2024 Financing, net proceeds of $35.2 million from the ATM Programs and proceeds from exercises of stock options and warrants of $4.8 million.

Net cash provided by financing activities was $88.4 million during the year ended December 31, 2023, which was attributable to net proceeds of $59.5 million from the October 2023 Financing, net proceeds of $28.5 million from the 2021 ATM Program and proceeds from exercises of stock options of $0.4 million.

Material Cash Requirements from Known Contractual Obligations

As of December 31, 2024, our only material contractual obligation was our sublease which commenced on June 1, 2024, pursuant to which we are required to make monthly payments of $0.1 million, effective September 1, 2024 until its expiration on November 30, 2028, in addition to payment obligations of $2.1 million if certain clinical milestones related to the ALPHA-ORBIT Phase 3 clinical trial of navenibart are met and payment obligations of $2.0 million if certain clinical milestones related to the Phase 1a clinical trial of STAR-0310 are met. The specified certain clinical milestones related to the Phase 1a clinical trials of STAR-0310 were met in January 2025.

We enter into agreements in the normal course of business with CROs for clinical trials, with third party manufacturers for clinical supplies and with vendors for preclinical research studies and other services and products for operating purposes. The contracts are cancelable at any time by us, generally upon 30 to 90 days' prior written notice to the counterparty, and we believe that our non-cancelable obligations under these agreements are not material.

Our license agreement with Ichnos, which covers STAR-0310, includes potential milestone payments, tiered royalties and other obligations that are dependent upon the development of products using the intellectual property licensed under the agreement and contingent upon the achievement of development or regulatory approval milestones, as well as commercial milestones. For further information regarding this agreement, please see Note 1, "*Nature of Business*" to our consolidated financial statements included in this Annual Report on Form 10-K. We are also party to a research services agreement, which covers navenibart, that includes the $2.1 million Phase 3 clinical trial milestone payment described above. The research services agreement also includes up to $5.2 million payable upon the achievement of certain regulatory milestones and up to $6.3 million payable upon the achievement of certain commercial milestones. The potential obligations in our license agreement and research service agreement are contingent upon future events and the timing and likelihood of such potential obligations are not known with certainty.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data

The consolidated financial statements together with the report of our independent registered public company accounting firm (PCAOB ID: 42) required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those consolidated financial statements is found in Item 15 of this Annual Report on Form 10-K.

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

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

As of December 31, 2024, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based

upon the evaluation described above that, as of December 31, 2024, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel 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 and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013). Based on its assessment, our management believes that, as of December 31, 2024, our internal control over financial reporting was effective based on those criteria.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting in accordance with an exemption established for smaller reporting companies with annual revenue of less than $100 million.

Changes in Internal Control over Financial Reporting

During the three months ended December 31, 2024, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (each as defined in Item 408 of Regulation S-K) during the fourth quarter of 2024.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is set forth under the captions "Election of Class I Directors — Information Regarding Directors," "Election of Class I Directors — Members of our Board of Directors Continuing in Office," "Executive Officers," "Corporate Governance — Code of Business Conduct and Ethics" "Corporate Governance — Director Nomination Process" "Corporate Governance — Committees of the Board of Directors — Audit Committee" and "Corporate Governance – Insider Trading Policy" in our definitive proxy statement for our 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024, and is incorporated into this Annual Report on Form 10-K by reference.

We are also required under Item 405 of Regulation S-K to provide information concerning delinquent filers of reports under Section 16 of the Securities Exchange Act of 1934, as amended. If applicable, this information will be set forth under the caption "Delinquent Section 16(a) Reports" in our definitive proxy statement for the 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024 and is incorporated into this Annual Report on Form 10-K by reference.

We have adopted a code of ethics, our Code of Business Conduct and Ethics, that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, and persons performing similar functions. Our Code of Business Conduct and Ethics, as well as our corporate governance guidelines and the charters for the audit, compensation, nominating and corporate governance, and science and technology committees of our Board of Directors, are each accessible under the "Corporate Governance" heading of the "For Investors" section of our website, http://www.astriatx.com. We also intend to disclose in the same location on our website, any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation

The information required by this Item is set forth under the captions "Executive Compensation" (except for the section titled "Executive Compensation — Pay Versus Performance")"Corporate Governance — Director Compensation" and "Corporate Governance — Policies and Procedures Related to the Grant of Certain Equity Awards" in our definitive proxy statement for our 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024, and is incorporated into this Annual Report on Form 10-K by reference.

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

The information required by this Item is set forth under the captions "Executive Compensation — Securities Authorized for Issuance under Equity Compensation Plans" and "Principal Stockholders" in our definitive proxy statement for our 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024, and is incorporated into this Annual Report on Form 10-K by reference.

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

The information required by this Item is set forth under the captions "Corporate Governance — Director Independence" and "Certain Relationships and Related Person Transactions" in our definitive proxy statement for our 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024, and is incorporated into this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item is set forth under the caption "Ratification of the Appointment of Ernst & Young LLP as Astria's Independent Registered Public Accounting Firm for the Fiscal Year Ending December 31, 2025" in our definitive proxy statement for our 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024, and is incorporated into this Annual Report on Form 10-K by reference.

PART IV

Item 15.

Exhibits and Financial Statement Schedules

(a)(1) Financial Statements

The financial statements listed below are filed as part of this Annual Report on Form 10-K and are incorporated herein by reference.

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(a)(2) Financial Statement Schedules

All financial schedules have been omitted because the required information is either presented in the consolidated financial statements filed as part of this Annual Report on Form 10-K or the notes thereto or is not applicable or required.

(a)(3) Exhibits

The exhibits required for this Annual Report on Form 10-K by Item 601 of Regulation S-K and Item 15(b) of Form 10-K are listed in the following Exhibit Index:

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, as amended (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on June 6, 2023)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on June 6, 2023)
4.1	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on October 12, 2023)
4.2	Form of Common Stock Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on October 12, 2023)
4.3	Description of Registered Securities (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form10-K (File No. 001-37467) filed with the SEC on March 10, 2022)
10.1*	Amended and Restated 2008 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.2*	Form of Incentive Stock Option Agreement under Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.3*	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.4*	Second Amended and Restated 2015 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on August 12, 2024)
10.5*	Form of Incentive Stock Option Agreement under Second Amended and Restated 2015 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on May 12, 2022)
10.6*	Form of Nonstatutory Stock Option Agreement under Second Amended and Restated 2015 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.6 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on May 12, 2022)
10.7*	2015 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on May 12, 2022)
10.8*	2022 Inducement Stock Incentive Plan, as amended (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on December 19, 2024)
10.9*	Form of Nonstatutory Stock Option Agreement under the 2022 Inducement Stock Incentive Plan, as amended (incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on February 22, 2022)
10.10*	Amended and Restated Employment Agreement, dated as of April 7, 2010, by and between the Registrant and Jill C. Milne, as amended (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.11*	Form of Amended and Restated Executive Severance Benefit Plan effective October 7, 2020 (incorporated by reference to Exhibit 10.8 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on May 12, 2022)
10.12+	License Agreement, dated as of October 4, 2023, by and between Ichnos Sciences SA, Ichnos Sciences Inc. and the Registrant (incorporated by reference to Exhibit 10.18 to the Registrant's Annual Report on Form 10-K (File No. 001-37467) filed with the SEC on March 4, 2024)
10.13	Sublease Agreement, dated as of January 3, 2024, by and between Duck Creek Technologies LLC and the Registrant (incorporated by reference to Exhibit 10.19 to the Registrant's Annual Report on Form 10 - K (File No. 001 - 37467) filed with the SEC on March 4, 2024)
19.1	Insider Trading Policy
21.1	Subsidiaries of the Registrant

23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
24.1	Power of Attorney (see signature page of this Annual Report on Form 10-K)
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
97.1	Compensation Recovery Policy of the Registrant (incorporated by reference to Exhibit 97.1 to the Registrant's Annual Report on Form 10-K (File No. 001-37467) filed with the SEC on March 4, 2024).
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Calculation Linkbase
101.LAB	XBRL Taxonomy Labels Linkbase Document
101.PRE	XBRL Taxonomy Presentation Linkbase Document
101.DEF	Taxonomy Extension Definition Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

* Management contract or compensatory plan arrangement.

\+ Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

Item 16. Form 10-K Summary

Not applicable.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Astria Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Astria Therapeutics, Inc. (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 two years in the period ended December 31, 2024, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

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

Navenibart Accrued and Prepaid Research and Development Costs

Description of the Matter

The Company's accrued contracted costs for research and development expenses totaled $6.2 million at December 31, 2024, including accruals related to the Company's Navenibart (STAR-0215) clinical trials. In addition, the Company's prepaid expenses and other current assets were $6.5 million and the Company's other non-current assets were $2.6 million, which included amounts that were paid in advance of services incurred pursuant to the Navenibart clinical trials. As discussed in Note 2 to the consolidated financial statements, the Company analyzes the progress of the clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the prepaid and accrued balances at the end of any reporting period for the Company's Navenibart clinical trials. The Company is required to estimate such prepaids and accruals using judgment based on certain information, including actual costs incurred or level of effort expended, as provided by its vendors. Payments for such activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheet within prepaid and other current assets or accrued expenses.

Auditing the Company's accrued and prepaid research and development costs for the Company's Navenibart clinical trials was complex, as accounting for the costs associated with the clinical trials requires subjective estimates of the level of services performed and the associated costs incurred by service providers. Furthermore, due to the duration of the Company's Navenibart clinical trials, and the timing of information received from third parties, the actual amounts incurred are not typically known at the time the consolidated financial statements are issued.

How We Addressed the Matter in Our Audit

To evaluate the accrued and prepaid research and development costs for the Navenibart clinical trials, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating the significant judgments and estimates made by management to determine the recorded accruals and prepayments. To test the significant judgments and estimates, we corroborated the progress of research and development activities through discussion with the Company's research and development personnel that oversee the research and development projects and inspected the Company's contracts with third parties and any pending change orders to assess the impact on amounts recorded. In addition, we inspected information obtained by the Company from third party vendors, which included the vendors' estimate of costs incurred to date. We obtained vendors direct confirmations to confirm cost incurred as of year-end to verify that accruals are complete and accurate. We also analyzed fluctuations in accruals by vendor and by program throughout the period subject to audit and tested subsequent invoices received from third party vendors.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2010.

Boston, Massachusetts

March 11, 2025

Astria Therapeutics, Inc.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 59,820	$ 175,530
Short-term investments	268,312	71,000
Prepaid expenses and other current assets	6,511	4,412
Total current assets	334,643	250,942
Right-of-use asset	5,114	363
Other assets	2,606	3,361
Total assets	$ 342,363	$ 254,666
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,320	$ 1,513
Accrued expenses	13,427	9,708
Current portion of operating lease liabilities	1,384	329
Total current liabilities	19,131	11,550
Long-term portion of operating lease liabilities	3,969	—
Total liabilities	23,100	11,550
Commitments (Note 6)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share, 4,908,620 shares authorized and no shares issued or outstanding	—	—
Series X redeemable convertible preferred stock, $0.001 par value per share, 91,380 shares authorized; 31,107 shares issued and outstanding as of December 31, 2024 and December 31, 2023, respectively	95,324	95,324
Common stock, $0.001 par value per share, 150,000,000 shares authorized; 56,434,219 and 41,034,797 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	57	41
Additional paid-in capital	898,513	728,285
Accumulated other comprehensive gain	163	—
Accumulated deficit	(674,794)	(580,534)
Total stockholders' equity	319,263	243,116
Total liabilities and stockholders' equity	$ 342,363	$ 254,666

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

Astria Therapeutics, Inc.
Consolidated Statements of Operations
(in thousands, except share and per share data)

	Year Ended December 31,	
	2024	**2023**
Operating expenses:		
Research and development	$ 77,106	$ 42,127
General and administrative	34,452	25,704
Acquired in-process research and development	—	15,199
Total operating expenses	111,558	83,030
Loss from operations	(111,558)	(83,030)
Other income (expense):		
Interest and investment income	17,360	10,201
Other expense, net	(62)	(62)
Total other income, net	17,298	10,139
Net loss	(94,260)	(72,891)
Net loss per share attributable to common shareholders - basic and diluted	$ (1.68)	$ (2.42)
Weighted-average common shares outstanding used in net loss per share - basic and diluted	56,161,249	30,123,316

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

Astria Therapeutics, Inc.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,	
	2024	**2023**
Net loss	$ (94,260)	$ (72,891)
Other comprehensive gain:		
Unrealized gain on short-term investments, net of tax of $0	163	79
Total other comprehensive gain:	163	79
Comprehensive loss	$ (94,097)	$ (72,812)

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

Astria Therapeutics, Inc.
Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	Series X redeemable convertible preferred stock, shares	Series X redeemable convertible preferred stock, value	Common stock, shares	Common stock, par value	Additional paid - in capital	Accumulated deficit	Accumulated other comprehensive loss	Total stockholders' equity
Balance at December 31, 2022	31,455	$ 96,398	27,501,340	$ 28	$ 632,512	$ (507,643)	$ (79)	$ 221,216
Issuance of common stock upon the conversion of preferred stock	(348)	(1,074)	57,910	—	1,074	—	—	—
Issuance of common stock and warrants pursuant to an underwriting agreement, net of underwriter's discount and issuance costs	—	—	8,253,895	8	59,472	—	—	59,480
Issuance of common stock for at-the-market offerings, net of issuance costs	—	—	4,738,606	5	28,493	—	—	28,498
Issuance of common stock upon exercise of options and warrants	—	—	483,046	—	420	—	—	420
Stock-based compensation expense	—	—	—	—	6,314	—	—	6,314
Unrealized gain on short-term investments	—	—	—	—	—	—	79	79
Net loss	—	—	—	—	—	(72,891)	—	(72,891)
Balance at December 31, 2023	31,107	95,324	41,034,797	41	728,285	(580,534)	—	243,116
Issuance of common stock pursuant to an underwriting agreement, net of underwriter's discount and issuance costs	—	—	10,340,000	10	117,162	—	—	117,172
Issuance of common stock for at-the-market offerings, net of issuance costs	—	—	4,450,425	5	35,240	—	—	35,245
Issuance of common stock upon exercise of options and warrants	—	—	608,997	1	4,784	—	—	4,785
Stock-based compensation expense	—	—	—	—	13,042	—	—	13,042
Unrealized gain on short-term investments	—	—	—	—	—	—	163	163
Net loss	—	—	—	—	—	(94,260)	—	(94,260)
Balance at December 31, 2024	31,107	$ 95,324	56,434,219	$ 57	$ 898,513	$ (674,794)	$ 163	$ 319,263

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

Astria Therapeutics, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2024	2023
Operating activities		
Net loss	$ (94,260)	$ (72,891)
Reconciliation of net loss to net cash used in operating activities:		
Stock-based compensation expense	13,042	6,314
Right-of-use asset- operating lease	1,004	585
Accretion of discount/premium on investment securities	(5,611)	(86)
Other non-cash items	70	46
Changes in assets and liabilities:		
Prepaid expenses and other assets	(1,252)	(4,546)
Lease liability - operating lease	(731)	(610)
Accounts payable	2,807	725
Accrued expenses	3,719	2,018
Net cash used in operating activities	(81,212)	(68,445)
Investing activities		
Purchases of short-term investments	(4,244,538)	(1,924,423)
Sales and maturities of short-term investments	4,053,000	2,059,500
Purchases of property and equipment	(325)	(25)
Net cash (used in) provided by investing activities	(191,863)	135,052
Financing activities		
Proceeds from public offering, net of underwriting discounts and issuance costs	117,172	59,480
Proceeds from at-the-market offering, net of issuance costs	35,245	28,498
Proceeds from exercise of stock options and warrants	4,785	420
Net cash provided by financing activities	157,202	88,398
Net (decrease) increase in cash, cash equivalents and restricted cash	(115,873)	155,005
Cash, cash equivalents and restricted cash, beginning of period	175,693	20,688
Cash, cash equivalents and restricted cash, end of period	$ 59,820	$ 175,693
Supplemental disclosure of non-cash transactions:		
Operating lease right-of-use assets obtained in exchange for operating lease liabilities	$ 5,753	$ —
Conversion of Series X Preferred Stock into common stock	$ —	$ 1,074
Purchases of property and equipment in accounts payable and accrued liabilities	$ —	$ 17
Public offering issuance costs in accrued expenses	$ —	$ 120

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

Astria Therapeutics, Inc.
Notes to Consolidated Financial Statements

1. Nature of Business

The Company

Astria Therapeutics, Inc. (the "Company"), is a biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for allergic and immunological diseases. The Company's lead product candidate is navenibart, formerly known as STAR-0215, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in clinical development for the treatment of hereditary angioedema ("HAE"), a rare, debilitating and potentially life-threatening disease. The Company's second product candidate is STAR-0310, a monoclonal antibody OX40 antagonist that is in preclinical development for the treatment of atopic dermatitis ("AD"), an immune disorder associated with loss of skin barrier function and itching. The Company was incorporated in the State of Delaware on June 26, 2008.

License Agreement

On October 4, 2023, the Company entered into a license agreement (the "Ichnos License Agreement") with Ichnos Sciences SA and Ichnos Sciences Inc. (collectively, "Ichnos") pursuant to which Ichnos granted to the Company an exclusive (even as to Ichnos and its affiliates), worldwide, and sublicensable right and license to certain patent rights and related know-how (collectively, the "Licensed Intellectual Property"), to develop, manufacture, and commercialize Ichnos' proprietary OX40 portfolio. The OX40 portfolio includes Ichnos' proprietary OX40 antagonist monoclonal antibody, with the generic name telazorlimab and also referred to by Ichnos as "ISB 830" as well as Ichnos' proprietary affinity matured next generation OX40 antagonist monoclonal antibody referred to by Ichnos as "ISB 830-X8" and referred to by the Company as "STAR-0310 candidate" (collectively, the "Licensed Compounds"). The Company agreed to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one product that contains or comprises a Licensed Compound (a "Licensed Product") in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan.

Under the terms of the Ichnos License Agreement, the Company paid Ichnos a one-time upfront license fee of $15.0 million in October 2023. The Company is obligated to pay Ichnos up to $305.0 million in milestones, consisting of up to $20.0 million upon the achievement of certain development milestones, up to $70.0 million upon the achievement of certain regulatory milestones and up to $215.0 million upon the achievement of certain commercial milestones, in each case in up to three indications with respect to the first applicable Licensed Product to achieve such milestone events. The Company is also obligated to pay Ichnos tiered royalties ranging from a mid-single-digit percentage to a low-double-digit percentage on aggregate annual net sales of all Licensed Products. The Company is obligated to pay royalties on a Licensed Product-by-Licensed Product and country-by-country basis until the latest of: (i) the expiration of the last valid claim covering the composition of matter of such Licensed Product in such country; (ii) the expiration of the last regulatory exclusivity with respect to such Licensed Product in such country; and (iii) twelve years following the first commercial sale of such Licensed Product in such country. The royalty rate is subject to reduction on a Licensed Product-by-Licensed Product and country-by-country basis under certain circumstances.

Liquidity

On October 16, 2023, the Company closed an underwritten offering (the "October 2023 Financing") of (i) 8,253,895 shares of common stock and accompanying common stock warrants to purchase an aggregate of 6,190,418 shares of common stock and (ii), in lieu of common stock to certain investors, pre-funded warrants to purchase up to an aggregate of 1,571,093 shares of common stock and accompanying common stock warrants to purchase up to an aggregate of 1,178,320 shares of common stock for aggregate gross proceeds of $64.0 million and net proceeds of $59.5 million. The October 2023 Financing included 2,727,340 shares of common stock, 3,223,824 common stock warrants and 1,571,093 pre-funded warrants issued to related parties.

On February 1, 2024, the Company closed an underwritten offering of 10,340,000 shares of its common stock (the "February 2024 Financing"). The gross proceeds of the February 2024 Financing were $125.0 million and net proceeds were $117.2 million.

In June 2021, the Company entered into an Open Market Sale Agreement℠ with Jefferies LLC ("Jefferies"), pursuant to which the Company could issue and sell shares of common stock under an at-the-market offering program (the "2021 ATM Program"), which was completed in the first quarter of 2024. In March 2024, the Company entered into a new Open Market Sale Agreement℠ with Jefferies, pursuant to which the Company is able to issue and sell up to $150.0 million of shares of common stock under an at-the-market offering program (the "2024 ATM Program" and collectively with the 2021 ATM Program, the "ATM Programs"). The Company pays Jefferies commissions of up to 3% of the gross proceeds from any common stock sold through the ATM Programs. During the year ended December 31, 2024, the Company sold an aggregate of 4,450,425 shares of common stock under the ATM Programs for gross proceeds of $36.2 million and net proceeds of $35.2 million.

During the year ended December 31, 2023, the Company sold an aggregate of 4,738,606 shares of common stock under the 2021 ATM Program for gross proceeds of $29.4 million and net proceeds of $28.5 million. As of December 31, 2024, the Company had an accumulated deficit of $674.8 million and had available cash, cash equivalents and short-term investments $328.1 million. The Company estimates its existing cash, cash equivalents, and short-term investments are sufficient to sustain operations for at least twelve months from the issuance of these consolidated financial statements.

The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities. There can be no assurance that the Company will be able to obtain additional debt, equity or other financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations, and financial condition. The Company is subject to a number of risks similar to other life science companies, including, but not limited to, successful discovery and development of its drug candidates, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology and regulatory approval and market acceptance of the Company's products. The Company has been primarily involved with research and development activities and has incurred operating losses and negative cash flows from operations since its inception. The Company anticipates that it will continue to incur significant operating losses for the next several years as it continues to develop its product candidates.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Astria Securities Corporation and Quellis Biosciences, LLC, successor in interest to Quellis Biosciences, Inc. All intercompany balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from such estimates.

The Company utilizes certain estimates to record expenses relating to research and development contracts and the valuation of stock-based awards and warrants. These contract estimates, which are primarily related to the length of service of each contract and the amount of service provided as of each measurement date, are determined by the Company based on input from internal project management, as well as from service providers.

Off-Balance Sheet Risk

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts or other foreign hedging arrangements.

Concentrations of Credit Risk and Significant Suppliers

Financial instruments that subject the Company to credit risk primarily consist of cash, cash equivalents, short-term investments and restricted cash. The primary objectives for the Company's investment portfolio are the preservation of capital and the maintenance of liquidity. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk.

The Company is dependent on third-party manufacturers and contract research organizations to supply products for research and development activities in its programs and to conduct clinical trials. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients, other raw materials, formulated drugs and drug-device combinations related to these programs in addition to reliance on the conduct of the clinical trial to be performed. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients, other raw materials and formulated drugs or an interruption in the provision of services provided by the Company's contract research organizations.

Cash and Cash Equivalents and Restricted Cash

The reconciliation of cash, cash equivalents and restricted cash reported within the applicable balance sheet that sum to the total of the same such amount shown in the statement of cash flows is as follows (in thousands):

	December 31,	
	2024	2023
Cash and cash equivalents	$ 59,820	$ 175,530
Restricted cash	—	163
Total	$ 59,820	$ 175,693

Short-Term Investments

The Company classifies all corporate debt securities with a remaining maturity of greater than three months and reverse repurchase agreements with a remaining maturity of greater than one business day at the time of purchase as short-term investments. Short-term investments are recorded at fair value, with the unrealized gains and losses reported in other comprehensive loss. The amortized cost of debt securities is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, interest, dividends and declines in value judged to be other-than-temporary are included in interest and investment income.

At each reporting date, the Company performs an evaluation of impairment to determine if any unrealized losses are the result of credit losses. Impairment is assessed at the individual security level. Factors considered in determining whether a loss resulted from a credit loss or other factors include the Company's intent and ability to hold the investment until the recovery of its amortized cost basis, the extent to which the fair value is less than the amortized cost basis, the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, any historical failure of the issuer to make scheduled interest or principal payments, any changes to the rating of the security by a rating agency, any adverse legal or regulatory events affecting the issuer or issuer's industry, and any significant deterioration in economic conditions.

The cost of securities sold is based on the specific identification method for purposes of recording realized gains and losses. To determine whether an other-than-temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary.

Fair Value of Financial Instruments

The fair value hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three broad levels as follows: Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities; Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The carrying amounts reflected in the balance sheets for cash equivalents, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at December 31, 2024 and 2023, due to their short-term nature. There have been no changes to the valuation methods during the years ended December 31, 2024 and 2023. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between levels during the years ended December 31, 2024 and 2023.

The Company's investment portfolio may include fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. The Company validates the prices provided by its third-party pricing services by obtaining market values from other pricing sources and analyzing pricing data in certain instances. The Company also invests in certain reverse repurchase agreements which are collateralized by deposits in the form of United States Government Securities and Obligations for an amount no less than 102% of their value. The Company does not record an asset or liability for the collateral as the Company is not permitted to sell or re-pledge the collateral. The collateral has at least the prevailing credit rating of United States Government Treasuries and Agencies. The Company utilizes a third-party custodian to manage the exchange of funds and ensure that collateral received is maintained at 102% of the value of the reverse repurchase agreements on a daily basis.

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. The Company has not recognized any significant impairment charges from inception through December 31, 2024.

Accrued and Prepaid Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include salaries and personnel-related costs, stock-based compensation, consulting fees, fees paid for contract research services, the costs of laboratory equipment and facilities and other external costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred. The deferred amounts are expensed as the related goods are delivered or the services are performed.

The Company records accruals for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances and prepaid balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation (*"ASC 718"). ASC 718 requires all share-based payments to employees, including grants of employee stock options, to be recognized in the statements of operations based on their grant date fair values. For granted stock options, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the Company's common stock consistent with the expected term of the option, risk-free interest rates and expected dividend yields of the Company's common stock.

For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period.

The Company expenses restricted stock awards based on the fair value of the award on a straight-line basis over the associated service period of the award.

Due to the lack of company-specific historical and implied volatility data of its common stock, the Company does not have sufficient relevant historical data to support its expected volatility. As such, the Company has used a weighted average of expected volatility based on a combination of the Company's own historical volatility and volatilities of a representative group of publicly traded biopharmaceutical companies. For purposes of identifying representative companies, the Company considered characteristics such as number of product candidates in early stages of product development, area of therapeutic focus, and length of trading history. The expected volatility was determined using the weighted average of the Company's own historical volatility and an average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to continue to consistently apply this process using the same representative companies until sufficient historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

The Company uses the "simplified method" to estimate the expected term of stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of the Company's stock options, taking into consideration multiple vesting tranches. The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's share-based awards.

The risk-free rate was based on the yield curve of United States Treasury securities with periods commensurate with the expected term of the options being valued.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. The Company has included pre-funded warrants to purchase 1,571,093 shares of common stock at an exercise price of $0.001 in its computation of basic net loss per share. Diluted net loss per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the Company's dilutive net loss per share attributable to common stockholders calculation, stock options and warrants to purchase the Company's common stock were considered to be common stock equivalents but were excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share attributable to common stockholders were the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2024	2023
Stock options	6,850,889	3,553,969
Common stock warrants	6,796,280	7,700,596
Series X Preferred Stock	5,184,591	5,184,591
	18,831,760	16,439,156

Income Taxes

The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more likely than not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC Topic 740, *Expenses—Income Taxes*. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company did not have any uncertain tax positions for any periods presented.

The Company assesses the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where it has operations to determine the potential effect on its business and any assumptions the Company has made about its future taxable income. The Company cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on its business if they were to be enacted. Beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminates the option to deduct research and development expenditures and requires taxpayers to amortize expense incurred in the United States over five years, and expense incurred outside of the United States over fifteen years. The United States Congress is considering legislation that would defer the amortization requirement to future periods, however, the Company has no assurance that the provision will be repealed or otherwise modified.

Segment Information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker, or CODM, in making decisions on how to allocate resources and assess performance. The CODM is the Company's Chief Executive Officer. The Company views its operations as and manages its business in one operating segment, focused on the discovery, development and commercialization of novel therapeutics for allergic and immunological diseases. The Company operates in one geographic segment. Segment information is further described in Note 11, "Segment Reporting".

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. Other comprehensive loss for all periods presented consists solely of unrealized gains (losses) on available-for-sale securities.

Leases

The Company determines if an arrangement is a lease at inception. Leases that are economically similar to the purchase of assets are generally classified as finance leases; otherwise the leases are classified as operating leases. The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew. Leases with a term greater than one year are recognized on the balance sheet as right-of-use ("ROU") assets, current portion of lease obligations, and long-term lease obligations. The Company does not currently hold any financing leases.

ROU lease assets represent the Company's right to use an underlying asset for the lease term and lease obligations represent the Company's obligation to make lease payments arising from the lease. Operating ROU lease assets and obligations are recognized at the commencement date based on the present value of lease payments over the lease term. However, certain adjustments to the ROU asset may be required for items such as incentives received. The Company has elected as an accounting policy to combine lease and non- lease components, such as common area maintenance, for all classes of underlying assets. As the Company's facility leases do not provide an implicit interest rate, the Company uses its estimated incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment at the commencement date. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

The Company's ROU lease assets also include any lease payments made and excludes lease incentives. The Company would recognize facility leases that include options to terminate the lease that would affect the lease period when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments under facility leases are recognized on a straight-line basis over the lease term.

Acquired In-Process Research and Development

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire in-process research and development ("IPR&D") with no alternative future use is charged to expense at the acquisition date. Refer to "License Agreement" below in this Note 2 for a more detailed description of the accounting policy utilized for the recent asset acquisition.

Preferred Stock Discount

In February 2021, the Company issued Series X Preferred Stock in a private placement transaction. It was determined that this transaction resulted in recognition of a beneficial conversion feature, which was valued based on the difference between the price of the shares of common stock on the date of commitment and the conversion price on the closing date, resulting in a total value of $19.6 million. Additionally, the Company incurred total issuance costs of $5.7 million related to the private placement. Both of these features were recorded as a discount on Series X Preferred Stock recognized at the close of the transaction. These features are analogous to preferred dividends and are recorded as a non-cash return to holders of Series X Preferred Stock through additional paid in capital. The discount related to the beneficial conversion feature is recognized through the earliest possible date of conversion, which occurred upon the stockholder approval of the conversion in June 2021. The issuance costs are recognized as a dividend at the time of conversion to common shares. As of December 31, 2024, $24.4 million of the above amounts were accounted for as a non-cash dividend related to shares of Series X Preferred Stock, and $0.9 million remained to be recognized upon future conversion.

License Agreement

On October 4, 2023, the Company entered into the Ichnos License Agreement, with Ichnos as discussed in Note 1, "Organization and Operations". Under the terms of the Ichnos License Agreement, the Company paid Ichnos a one-time upfront license fee of $15.0 million in October 2023. The Company concluded that the Ichnos License Agreement was not the acquisition of a business, as substantially all of the fair value of the gross assets acquired was concentrated in a single identifiable asset "ISB 830-X8", referred to by the Company as the STAR-0310 candidate. STAR-0310 is STAR-0310 candidate engineered with YTE half-life extension technology.

The Company determined that the cost to acquire the Licensed Intellectual Property assets was $15.2 million, primarily based on the fair value of the upfront license fee of $15.0 million and external legal fees of $0.2 million attributable to the acquired IPR&D. As the STAR-0310 candidate had not, at the time of the Ichnos License Agreement, received regulatory approval in any territory, the cost attributable to the IPR&D was expensed in the Company's consolidated statements of operations and comprehensive loss for the year ended December 31, 2023 as the acquired IPR&D had no alternative future use, as determined by the Company in accordance with U.S. GAAP.

Financing Costs

Costs incurred in connection with the issuance of equity units and shares are recorded as a reduction of proceeds to the equity carrying value. The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process financings as deferred offering costs until such financings are consummated. After consummation of the financing, these costs are recorded as a reduction of the proceeds received from the financing. If a planned financing is abandoned, the deferred offering costs are expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. There were no deferred offering costs on the Company's consolidated balance sheet at December 31, 2024 and December 31, 2023.

Recently Adopted Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies and adopted by the Company as of the specified effective date.

In August 2020, the FASB issued Accounting Standards Update 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging Contracts in Entity's Own Equity (Subtopic 815-40)* ("ASU 2020-06"), which reduced the number of accounting models for convertible debt instruments and convertible preferred stock as well as amended the derivatives

scope exception for contracts in an entity's own equity. ASU 2020-06 was effective for the Company for the fiscal year beginning on January 1, 2024, with early adoption permitted. The Company adopted this standard on January 1, 2024 with no material impact on the consolidated financial statements.

In November 2023, the FASB issued Accounting Standards Update 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"). The amendments in this update improve reportable segment disclosure requirements through enhanced disclosures about significant segment expenses. All disclosure requirements of the update are required for entities with a single reportable segment. The amendments were effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, and are required to be applied on a retrospective basis to all periods presented. Refer to Note 11, "Segment Reporting", for additional disclosures related to this new standard.

Recently Issued Accounting Pronouncements – Not Yet Adopted

In October 2023, the FASB issued Accounting Standards Update 2023-06, *Disclosure Improvements: Codification Amendments in Response to the SEC's Disclosure Update and Simplification Initiative* ("ASU 2023-06"), which incorporates certain United States Securities and Exchange Commission ("SEC") disclosure requirements into the Accounting Standards Codification ("ASC"). The amendments in ASU 2023-06 are expected to clarify or improve disclosure and presentation requirements of a variety of topics, allow investors to more easily compare entities subject to the SEC's existing disclosure requirements with those entities that were not previously subject to the requirements, and align the requirements in the ASC with the SEC's regulations. The effective date for each amendment will be the date on which the SEC's removal of that related disclosure from Regulation S-X or Regulation S-K becomes effective, with early adoption prohibited. The amendments in ASU 2023-06 should be applied prospectively. The Company is currently evaluating this guidance to determine the impact it may have on its consolidated financial statements.

In December 2023, the FASB issued Accounting Standards Update 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"). This guidance is intended to enhance the transparency and decision-usefulness of income tax disclosures. The amendments in ASU 2023-09 address investor requests for enhanced income tax information primarily through changes to disclosure regarding rate reconciliation and income taxes paid both in the United States and in foreign jurisdictions. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024 on a prospective basis, with the option to apply the standard retrospectively. Early adoption is permitted. The Company is currently evaluating this guidance to determine the impact it may have on its consolidated financial statement disclosures.

In November 2024, the FASB issued Accounting Standards Update 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"). The amendments in ASU 2024-03 require public entities to disclose in a tabular format, on an annual and interim basis, the amounts of inventory purchases, employee compensation, depreciation and intangible asset amortization included in each income statement line item that contains those expenses. In January 2025, the FASB issued Accounting Standards Update 2025-01, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40)* ("ASU 2025-01"). ASU 2025-01 amends the effective date of ASU 2024-03 to clarify that all public business entities are required to adopt the guidance in annual reporting periods beginning after December 15, 2026, and interim periods within annual reporting periods beginning after December 15, 2027. Early adoption of ASU 2024-03 is permitted. The Company is currently evaluating this guidance to determine the impact it may have on its consolidated financial statement disclosures.

3. Fair Value Measurements

The following tables present information about the Company's financial assets and liabilities that have been measured at fair value and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value. During the years ended December 31, 2024 and 2023, there were no transfers between Level 1, Level 2 and Level 3.

Below is a summary of assets and liabilities measured at fair value on a recurring basis (in thousands):

	As of December 31, 2024			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	$ 30,610	$ —	$ —	$ 30,610
Short-term investments:				
Treasury notes	129,197	—	—	129,197
Reverse repurchase agreements	—	100,000	—	100,000
Treasury bills	39,115	—	—	39,115
Total	$ 198,922	$ 100,000	$ —	$ 298,922

	As of December 31, 2023			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	$ 7,709	$ —	$ —	$ 7,709
Short-term investments:				
Reverse repurchase agreements	—	71,000	—	71,000
Total	$ 7,709	$ 71,000	$ —	$ 78,709

At December 31, 2024 and 2023, cash equivalents approximated their fair value due to their short-term nature.

4. Short-Term Investments

The following tables summarize short-term investments (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2024				
Treasury notes	$ 129,064	$ 136	$ (3)	$ 129,197
Reverse repurchase agreements	100,000	—	—	100,000
Treasury bills	39,085	31	(1)	39,115
Total	$ 268,149	$ 167	$ (4)	$ 268,312

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2023				
Reverse repurchase agreements	$ 71,000	$ —	$ —	$ 71,000
Total	$ 71,000	$ —	$ —	$ 71,000

The contractual maturities of all short-term investments held at December 31, 2024 and December 31, 2023 were one year or less. There were two short-term investments in an unrealized loss position at December 31, 2024 with an aggregate value of $9.8 million. There were no short-term investments in an unrealized loss position at December 31, 2023. These investments were in a loss position for less than 12 months and the Company considered the loss to be temporary in nature. The Company considered the decline in market value for these securities to be primarily attributable to economic and market conditions.

Gross realized gains and losses on the sales of short-term investments are included in other income, net. Unrealized holding gains or losses for the period that have been included in accumulated other comprehensive income, as well as gains and losses reclassified out of accumulated other comprehensive income into other income, net, were not material to the Company's consolidated results of operations. The cost of investments sold or the amount reclassified out of the accumulated other comprehensive income into other income, net is based on the specific identification method for purposes of recording realized gains and losses. All proceeds in the years ended December 31, 2024 and 2023 related to maturities of underlying investments. The gains on proceeds from maturities of short-term investments were not material to the Company's consolidated results of operations for the years ended December 31, 2024 and 2023.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Accrued contracted costs	$ 6,187	$ 3,861
Accrued compensation	5,084	4,047
Accrued professional fees	1,963	1,485
Accrued other	193	315
Total	$ 13,427	$ 9,708

6. Commitments

On January 3, 2024, the Company entered into a sublease agreement (the "Sublease") with Duck Creek Technologies LLC to occupy 30,110 square feet of office space in Boston, Massachusetts to replace its existing office space. The Sublease commenced on June 1, 2024 and will end on November 30, 2028 (or on such earlier date as the term may cease or expire as set forth in the Sublease). The Company concluded that the Sublease was an operating lease and recognized a lease liability and right-of-use ("ROU") asset of approximately $5.8 million at the inception of the Sublease. The lease liability represents the present value of the remaining lease payments, discounted using the Company's estimated incremental borrowing rate of 7.49%. The ROU asset represents the lease liability adjusted for any prepaid and accrued rent payments. The Sublease is secured by a security deposit of $0.4 million. As of December 31, 2024, the remaining lease term of the Sublease was 3.9 years. As of December 31, 2024, minimum lease payments under the Company's operating leases are summarized as follows (in thousands):

Period Ending December 31,	Amount
2025	1,446
2026	1,608
2027	1,640
2028	1,531
Total lease payments	$ 6,225
Less: imputed interest	(872)
Total operating lease liabilities	$ 5,353

Rent expense was $1.3 million and $0.6 million for the years ended December 31, 2024 and 2023, respectively. Lease payments were $1.0 million and $0.7 million for the years ended December 31, 2024 and 2023, respectively.

7. Stockholders' Equity

Preferred Stock

Under the Company's amended and restated certificate of incorporation, the Company has 5,000,000 shares of preferred stock authorized for issuance, with a $0.001 par value per share. Preferred stock may be issued from time to time in one or more series, each series to have such terms as stated or expressed in the resolutions providing for the issue of such series adopted by the board of directors of the Company (the "Board of Directors"). Preferred stock which may be redeemed, purchased or acquired by the Company may be reissued except as otherwise provided by law. As of December 31, 2024, the Company had 31,107 shares of Series X Preferred Stock outstanding. Each share of Series X Preferred Stock is convertible into 166.67 shares of common stock and therefore the number of shares of underlying common stock issuable upon conversion of the Series X Preferred Stock is 5,184,591.

Outstanding Warrants

The Company accounted for warrants to purchase its stock pursuant to ASC Topic 470, *Debt*, and ASC Topic 480, *Distinguishing Liabilities from Equity*, and classifies warrants for common stock and preferred stock as liabilities or equity. Warrants classified as liabilities are reported at their estimated fair value and any changes in fair value are reflected in research and development expense. Warrants classified as equity are reported at their estimated fair value with no subsequent remeasurement. As of December 31, 2024 and 2023, all outstanding warrants were classified as equity.

The following table presents information about warrants that are issued and outstanding at December 31, 2024:

Year Issued	Equity Instrument	Warrants Outstanding	Exercise Price	Date of Expiration
2023 (1)	Common Stock	6,796,280	$ 8.03	10/16/2028
Total		6,796,280		
Weighted average exercise price			$ 8.03	
Weighted average life in years				3.79

(1) 1,571,093 pre-funded warrants were issued in 2023 with an exercise price of $0.001 per share and are exercisable until all pre-funded warrants are exercised in full. 1,571,093 pre-funded warrants were outstanding as of December 31, 2024 and are not included in the table above.

Common Stock

As of December 31, 2024, the Company had 150,000,000 shares of common stock authorized for issuance, $0.001 par value per share, with 56,434,219 shares issued and outstanding. The voting, dividend and liquidation rights of holders of common stock are subject to and qualified by the rights, powers and preferences of the holders of any outstanding preferred stock.

Reserved for Future Issuance

The Company has reserved the following shares of common stock for future issuance:

	December 31, 2024	December 31, 2023
Reserved under the 2015 Second Amended and Restated Stock Incentive Plan and the 2022 Inducement Stock Incentive Plan	8,849,170	5,334,301
Warrants for the purchase of common stock	8,367,373	9,271,689
Options outstanding to purchase common stock	6,850,889	3,553,969
Series X Preferred Stock	5,184,591	5,184,591
Reserved under the employee stock purchase plan	49,139	43,060
Total	29,301,162	23,387,610

8. Stock-Based Compensation

2015 Second Amended and Restated Equity Incentive Plan

Prior to the Company's initial public offering in June 2015 (the "IPO"), the Company granted awards to eligible participants under its 2008 Equity Incentive Plan. In May 2015, the Board of Directors adopted and, in June 2015, the Company's stockholders approved the 2015 Stock Incentive Plan, as amended and amended and restated since the IPO ("2015 Plan"), which became effective immediately prior to the effectiveness of the IPO. Subsequent to the IPO, no option grants have been awarded to eligible participants under the 2008 Equity Incentive Plan.

The 2015 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2015 Plan.

Terms of stock option agreements, including vesting requirements, are determined by the Company's board of directors, subject to the provisions of the applicable stock incentive plan. Options granted by the Company generally vest ratably over four years, with a one-year cliff, and options are exercisable from the date of grant for a period of ten years. As of December 31, 2024, options to purchase 5,378,672 shares of common stock are outstanding and 7,554,324 shares of common stock remain available for issuance under the 2015 Plan, all of which shares of common stock are reserved for issuance.

2022 Inducement Stock Incentive Plan

On February 17, 2022, the Board of Directors adopted the 2022 Inducement Stock Incentive Plan (the "Inducement Plan"). The Inducement Plan provides for the grant of nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards with respect to an aggregate of 300,000 shares of the Company's common stock. Awards under the Inducement Plan may only be granted to persons who (a) were not previously an employee or director of the Company or (b) are commencing employment with the Company following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with the Company and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4).

The Board of Directors approved amendments to the Inducement Plan to increase the number of shares of common stock authorized for issuance by 1,400,000 shares of common stock in the year ended December 31, 2023 and 1,100,000 shares of common stock in the year ended December 31, 2024. As of December 31, 2024, options to purchase 1,472,217 shares of common stock are outstanding and 1,294,846 shares of common stock remain available for issuance under the Inducement Plan, all of which shares of common stock are reserved for issuance.

Stock Option Activity

A summary of the Company's stock option activity and related information for employees and non-employees follows:

	Shares	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2023	3,553,969	$ 13.59	8.39	$ 1,912
Granted	3,644,675	$ 13.90		
Exercised	(36,539)	$ 5.21		
Cancelled or forfeited	(309,544)	$ 12.52		
Expired	(1,672)	$ 414.04		
Outstanding at December 31, 2024	6,850,889	$ 13.75	8.31	$ 2,946
Vested and exercisable at December 31, 2024	2,206,580	$ 15.15	7.05	$ 1,878
Vested and expected to vest at December 31, 2024	6,850,889	$ 13.75	8.31	$ 2,946

The total intrinsic value of options exercised in the years ended December 31, 2024 and 2023 was $0.2 million and $0.5 million, respectively. The total grant date fair value of stock options vested for the year ended December 31, 2024 and 2023 was $8.6 million and $4.4 million, respectively. The weighted-average grant date fair value of options granted to employees and non-employees for the years ended December 31, 2024 and 2023 was $9.51 and $7.20 per share, respectively.

At December 31, 2024, the total unrecognized compensation expense related to unvested stock option awards was $33.2 million. The Company expects to recognize that cost over a weighted-average period of approximately 2.9 years.

Stock-Based Compensation Expense

During the years ended December 31, 2024 and 2023, the Company recorded stock-based compensation expense for employee and non-employee stock options and restricted stock, which was allocated as follows in the statements of operations (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development	$ 3,782	$ 1,304
General and administrative	9,260	5,010
Total	$ 13,042	$ 6,314

No related tax benefits were recognized for the years ended December 31, 2024 and 2023.

The fair value of stock options granted to employees and non-employees was estimated using the Black-Scholes option-pricing model based on the following assumptions:

	Year Ended December 31,	
	2024	2023
Weighted-average expected volatility	74.32%-76.4%	65.86%-73.68%
Expected term (in years)	5.5-6.25	5.5-6.25
Risk-free interest rate	3.53%-4.59%	3.42%-4.67%
Expected dividend yield	0%	0%

9. Income Taxes

For the years ended December 31, 2024 and 2023, the Company did not record a provision for federal or state income taxes as it has incurred cumulative net operating losses since inception.

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
	2024	2023
Federal income tax (benefit) at statutory rate	21.00 %	21.00 %
Permanent differences	(0.07)	(0.12)
Federal research and development credits and adjustments	5.43	3.44
State income tax, net of federal benefit	6.34	6.25
Stock compensation	(1.76)	(1.61)
Other	(0.39)	0.05
Change in valuation allowance	(30.55)	(29.01)
Effective income tax rate	— %	— %

The Company's deferred tax assets consisted of the following (in thousands):

	Year Ended December 31,	
	2024	2023
Deferred tax assets		
Net operating loss carryforwards	$ 93,650	$ 85,734
Tax credit carryforwards	19,719	14,576
Capitalized research and development	31,719	16,927
Capitalized licenses	3,714	4,041
Capitalized legal expenses	816	918
Lease liability	1,442	90
Other differences	3,846	2,587
Total gross deferred tax assets	154,906	124,873
Less valuation allowance	(153,529)	(124,774)
Net deferred tax assets	1,377	99
Deferred tax liabilities		
ROU asset	(1,377)	(99)
Net deferred taxes	$ —	$ —

For taxable years beginning after December 31, 2021, the Tax Cuts and Jobs Act (the "Tax Act") eliminated the option to deduct research and development expenditures in the current year and requires taxpayers to capitalize such expenses pursuant to the Internal Revenue Code of 1986, as amended ("IRC") Section 174. As a result of this provision of the Tax Act, deferred tax assets related to capitalized research expenses pursuant to IRC Section 174 increased to approximately $31.7 million for the year ended December 31, 2024, and $16.9 million for the year ended December 31, 2023.

The Company recorded an increase to the valuation allowance of $28.8 million during the year ended December 31, 2024 due primarily to the federal and state net operating losses and tax credits generated in the current year. The Company recorded an increase to the valuation allowance of $21.1 million during the year ended December 31, 2023, which was also primarily due to the federal and state net operating losses, and tax credits generated.

In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Due to the Company's history of losses and expectation of future losses, the deferred tax assets were fully offset by a valuation allowance at December 31, 2024 and 2023.

As of December 31, 2024, the Company had approximately $340.8 million of federal and $349.5 million of state net operating loss respectively, which may be available to offset future taxable income, if any, of which $150.6 million of federal and $349.5 million of state carryforwards will expire at various dates from 2028 through 2044. Additionally, $190.2 million of federal net operating loss carryforwards will carry forward indefinitely. The Company had $16.4 million of federal and $4.2 million of state tax credit carryforwards available to reduce future tax liabilities as of December 31, 2024, which will expire at varying times through the year 2044.

The IRC provides for a limitation of the annual use of net operating losses and other tax attributes (such as research and development tax credit carryforwards) following certain ownership changes (as defined by the IRC) that could limit the Company's ability to utilize these carryforwards. The Company has completed a study through December 31, 2022 to assess whether an ownership change under Section 382 of the IRC has occurred and as a result the Astria federal and state net operating loss and research and development credit carryforwards are significantly limited for use. Accordingly, the Company's ability to utilize the aforementioned carryforwards are limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. Therefore, the Company will not be able to take full advantage of all of its current carryforwards for federal or state income tax purposes.

As of December 31, 2024 and 2023, the Company did not have any significant unrecognized tax benefits. Interest and penalty charges, if any, related to uncertain tax positions would be classified as income tax expenses in the accompanying consolidated statements of operations. The Company has not had any accrued interest or penalties related to uncertain tax positions.

The federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2021 through December 31, 2024. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state taxing authorities to the extent utilized in a future period.

10. Defined Contribution Benefit Plan

The Company offers a defined-contribution savings plan under Section 401(k) of the IRC., in which substantially all of its employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. In 2023, the Company matched 100% of an employee's 401(k) contributions up to $4,000. Beginning on January 1, 2024, the Company matched the higher of: 100% of an employee's 401(k) contributions up to $4,000 or 50% of an employee's 401(k) contributions up to a maximum of 5% of the participant's salary, subject to employer match limitations under the IRC. The Company provided $0.4 million and $0.2 million in matching contributions during the years ended December 31, 2024 and 2023, respectively.

11. Segment Reporting

The Company operates and manages its business as one reportable segment and one operating segment focused on the discovery, development and commercialization of novel therapeutics for allergic and immunological diseases. The CODM assesses performance for the segment and decides how to allocate resources based on consolidated net loss that is also reported on the consolidated statements of operations.

The measure of segment assets is reported on the consolidated balance sheets as total consolidated assets. All material long-lived assets are located in the United States. Long-lived assets consist of property and equipment, net, and operating lease right-of-use assets.

The CODM uses consolidated net loss to evaluate the Company's spend and monitor budget versus actual results. The monitoring of budgeted versus actual results is used in assessing performance of the segment and in establishing resource allocation across the organization.

Factors used in determining the reportable segment include the nature of the Company's operating activities, the organizational and reporting structure and the type of information reviewed by the CODM to allocate resources and evaluate financial performance. The accounting policies of the segment are the same as those described in Note 2, "Summary of Significant Accounting Policies".

The following table presents reportable segment profit and loss, including significant expense categories, attributable to the Company's reportable segment for the periods presented:

	Year Ended December 31,	
	2024	2023
Expenses[1]:		
Research and development:		
Navenibart	$ 32,401	$ 24,186
STAR-0310	15,497	677
Employee expenses	14,415	9,859
General and administrative:		
Program support[2]	1,021	476
Employee expenses	11,575	9,128
Stock-based compensation expense	12,907	6,313
Consulting and professional services expenses	17,952	9,382
Other segment expenses[3]	5,790	7,810
Acquired in-process research and development[4]	—	15,199
Other income, net[5]	(17,298)	(10,139)
Segment net loss	$ 94,260	$ 72,891

(1) The significant expense categories and amounts align with segment level information that is regularly provided to the CODM.

(2) General and administrative program support expense includes commercial costs incurred in support of navenibart and STAR-0310, and patient advocacy costs incurred in support of navenibart and STAR-0310.

(3) Other segment expense includes: costs incurred in support of overall research and development activities and non-specific programs, facilities expense, office expense, insurance expense and depreciation and amortization.

(4) Acquired in-process research and development includes expense associated with entering into a license agreement as discussed in Note 1, “Organization and Operations”.

(5) Other income, net, consists primarily of interest income on investments, as further described in Note 4, “Short-Term Investments”. For the years ended December 31, 2024 and 2023, the Company recognized interest income of $17.4 million and $10.2 million, respectively.

12. Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence for certain estimates and to identify matters that require additional disclosure. Subsequent events have been evaluated as required.

SIGNATURES

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

Astria Therapeutics, Inc.

Date: March 11, 2025

By: /s/ Jill C. Milne
Jill C. Milne
President and Chief Executive Officer

We, the undersigned directors and officers of Astria Therapeutics, Inc. (the "Company"), hereby severally constitute and appoint Jill C. Milne and Noah Clauser, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

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

Signature	Title	Date
/s/ Jill C. Milne Jill C. Milne	President and Chief Executive Officer and Director (Principal Executive Officer)	March 11, 2025
/s/ Noah Clauser Noah Clauser	Chief Financial Officer and Treasurer (Principal Financial Officer, Principal Accounting Officer)	March 11, 2025
/s/ Kenneth Bate Kenneth Bate	Chairman	March 11, 2025
/s/ Sunil Agarwal Sunil Agarwal	Director	March 11, 2025
/s/ Joanne Beck Joanne Beck	Director	March 11, 2025
/s/ Frederick C. Callori Frederick C. Callori	Director	March 11, 2025
/s/ Hugh Cole Hugh Cole	Director	March 11, 2025
/s/ Michael Kishbauch Michael Kishbauch	Director	March 11, 2025
/s/ Gregg Lapointe Gregg Lapointe	Director	March 11, 2025
/s/ Jonathan Violin Jonathan Violin	Director	March 11, 2025

Directors (as of April 28, 2025)	Executive Officers (as of April 28, 2025)
Kenneth Bate, Chair of the Board of Directors, Astria Therapeutics, Inc., and independent consultant in the biotechnology field	Jill C. Milne, Ph.D., Co-Founder, Chief Executive Officer and President
Joanne Beck, Ph.D., former Chief Technology Officer, Abata Therapeutics, Inc.	Noah Clauser, Chief Financial Officer
Fred Callori, Partner and Managing Director, Perceptive Advisors	Benjamin Harshbarger, Chief Legal Officer
Hugh Cole, former Chief Operating Officer, Jounce Therapeutics, Inc., and independent consultant in the biotechnology field	Andrew A. Komjathy, Chief Commercial Officer
Michael Kishbauch, former President and Chief Executive Officer, Achillion Pharmaceuticals, Inc.	Andrea Matthews, Chief Business Officer
Gregg Lapointe, Co-Founder and Chief Executive Officer, Cerium Pharmaceuticals, Inc.	Christopher Morabito, M.D., Chief Medical Officer
Jill C. Milne, Ph.D., Co-Founder, Chief Executive Officer and President, Astria Therapeutics, Inc.	
Jonathan Violin, Ph.D., Venture Partner at Fairmount Funds Management, LLC	
Sunil Agarwal, M.D., former Executive Vice President and Chief Development Officer, Sana Biotechnology, Inc.	

Stockholder Information Requests

Stockholders who desire information about Astria Therapeutics, Inc. may contact us at 22 Boston Wharf Road, 10th Floor, Boston, MA 02210, Attention: Chief Business Officer (telephone: 617-349-1971; email: investors@astriatx.com). Information of interest to stockholders and investors, such as our annual reports, quarterly reports, proxy statements, press releases, and other information, is available on our website at www.astriatx.com under "For Investors."

Stock Transfer Agent

Equiniti Trust Company, LLC is the stock transfer agent for our common stock and maintains common stockholder activity records. Equiniti Trust Company, LLC will respond to questions on issuance of common stock certificates, change of ownership, lost common stock certificates, and changes of address. For these and similar matters, please direct inquiries to: Equiniti Trust Company, LLC, ATTN: Shareholders Services Dept., P.O. Box 500, Newark NJ 07101 (telephone: 800-937-5449) Email address: helpAST@equiniti.com or visit https://equiniti.com/us/ast-access/individuals/ for further instructions.

2025 Annual Meeting of Stockholders

Our 2025 Annual Meeting of Stockholders is scheduled to be held in person at the offices of Astria Therapeutics, Inc. at 22 Boston Wharf Road, 10th Floor, Boston, MA 02210 on June 11, 2025, at 8:00 a.m. Eastern Time. We will issue a press release and make a public filing with the U.S. Securities and Exchange Commission announcing any changes to the 2025 Annual Meeting, and we will also announce any changes at www.ir.astriatx.com. We encourage you to check this website prior to the 2025 Annual Meeting if you are considering attending.

Forward-Looking Statements

This annual report contains forward-looking statements within the meaning of applicable federal securities laws and regulations. Any statements contained in this annual report that are not statements of historical fact may be deemed to be forward-looking statements, including our expectations regarding: our projected cash runway; the potential significance of the initial results from the ALPHA-STAR Phase 1b/2 clinical trial of navenibart and the anticipated nature and timing of receipt of the data from additional cohorts in such trial; our plans and timing for the long-term open label study of navenibart; our longer term development plans for navenibart, including the anticipated nature and timing of results from the ALPHA-ORBIT Phase 3 pivotal trial; the potential attributes and differentiated profile of navenibart as a treatment for HAE, including those suggested by the preliminary and initial results from the navenibart Phase 1a trial, the ALPHA-STAR Phase 1b/2 trial, and market research; our goals and vision for navenibart; the potential commercial opportunity for navenibart in HAE and the likelihood that it can effectively compete in HAE, assuming it is approved; the need for effective treatments for HAE; the potential for three- to six-month dosing of navenibart; our goals and vision for STAR-0310; our longer term development plans for STAR-0310, including our plan to initiate a Phase 1b2 clinical trial of STAR-0310 following regulatory clearance; the potential attributes and differentiated profile of STAR-0310 as a treatment for AD; the potential for STAR-0310 to expand into additional indications; the nature, and significance of preclinical data related to STAR-0310; the timing of regulatory filings related to STAR-0310; the timing, nature and significance of the anticipated results of the Phase 1a clinical trial of STAR-0310; the potential commercial opportunity for STAR-0310 in AD and the likelihood that it can effectively compete in AD, assuming it is approved; the need for effective treatments for AD; and the Company's goal to meet the unmet needs of patients with allergic and immunological diseases. Without limiting the foregoing, the words "believes," intends," "anticipates," "plans," "expects," "seeks," "estimates," "would," "should," "likely," "will," "may," "continue," "could," "vision," or similar expressions are intended to identify forward-looking statements. While we may elect to update forward-looking statements in the future, we specifically disclaim any obligation to do so, even if our expectations change. A number of factors could cause our results to differ materially from those indicated by such forward-looking statements, including those detailed under the heading "Risk Factors" in Part 1, Item 1A in the accompanying Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and our subsequent filings with the U.S. Securities and Exchange Commission.