

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

FORM 10-K

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

For the fiscal year ended December 31, 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: 001-42143

Alumis Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State of other jurisdiction of incorporation or organization)

86-1771129

(I.R.S. Employer Identification Number)

280 East Grand Avenue

South San Francisco, CA 94080

(Address of Principal Executive Offices)

(650) 231-6625

(Registrant's telephone number)

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

| <u>Title of Each Class</u> | <u>Trading Symbol(s)</u> | <u>Name Of Each Exchange On Which Registered</u> |
|---|--------------------------|--|
| Common Stock, \$0.001 Par Value per Share | ALMS | The Nasdaq Global Select Market |

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.

Yes No

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

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.0405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company Emerging growth company

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

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

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

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

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

Based on the closing price as reported on the Nasdaq Global Select Market, the aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates on June 30, 2024 (the last business day of the registrant's most recently completed second fiscal quarter) plus the aggregate amount of gross proceeds received from the registrant's initial public offering from non-affiliates was approximately \$165.4 million. Shares of common stock held by each executive officer and director and by each stockholder affiliated with a director or an executive officer have been excluded from this calculation because such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. As of March 12, 2025, the registrant had 47,222,419 shares of voting common stock, \$0.0001 par value per share, and 7,184,908 shares of non-voting common stock, \$0.0001 par value per share, outstanding.

Documents Incorporated by Reference

Certain information required by Part III, Items 10-14 of this Form 10-K is incorporated by reference to the registrant's definitive Proxy Statement for the 2025 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A. If such Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Form 10-K, such information will be included in an amendment to this Form 10-K to be filed within such 120-day period.

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In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to “Alumis,” “the Company,” “we,” “us,” “our” and similar references refer to Alumis Inc.

This Annual Report on Form 10-K also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing in this report are the property of their respective holders. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

These forward-looking statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our expectations regarding the potential benefits of our strategy;
- our expectations regarding the announced merger transaction with ACELYRIN, Inc. ("ACELYRIN");
- our expectations regarding the operation of our product candidates and related benefits;
- the success of competing therapies that are, or may become, available;
- developments related to our competitors and our industry, including competing product candidates and therapies;
- details regarding our strategic vision and planned product candidate pipeline;
- our beliefs regarding the success, cost and timing of our product candidate development activities and current and future clinical trials and studies including study design;
- the timing or likelihood of regulatory filings or other actions and related regulatory authority responses;
- the ability and willingness of various third parties to engage in research and development activities involving our product candidates, and our ability to leverage those activities;
- our expectations regarding the ease of administration associated with our product candidates;
- our expectations regarding the patient compatibility associated with our product candidates;
- our beliefs regarding the potential markets for our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our ability to commercialize any approved products;
- the rate and degree of market acceptance of any approved products;
- our ability to attract and retain key personnel;

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- the accuracy of our estimates regarding our future revenue, as well as our future operating expenses, capital requirements and needs for additional financing;
- our ability to obtain funding for our operations, including funding necessary to complete further development and any commercialization of our product candidates;
- our ability to obtain, maintain, protect and enforce intellectual property protection for our product candidates and technology and not infringe, misappropriate or otherwise violate the intellectual property of others;
- regulatory developments in the United States and foreign countries;
- our expectations regarding the period during which we qualify as an “emerging growth company” under the Jumpstart Our Business Startups Act of 2012, as amended (the “JOBS Act”), and a “smaller reporting company,” as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”); and
- statements of belief and any statement of assumptions underlying any of the foregoing.

You should refer to the section titled “Risk Factors” in Part I, Item 1A. of this Annual Report on Form 10-K for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report on Form 10-K will prove to be accurate.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely upon these statements.

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

RISK FACTORS SUMMARY

Below is a summary of the material factors that make an investment in our securities speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this Risk Factors Summary, and other risks that we face, can be found below under the heading “Risk Factors” under Part I, Item 1A. of this Annual Report on Form 10-K and should be carefully considered, together with other information in this Annual Report on Form 10-K, before making investment decisions regarding our securities.

- The Merger (as defined herein) may not be completed on the terms or timeline currently contemplated, or at all. Our stockholders and ACELYRIN stockholders will be subject to a number of material risks if the Merger is not completed on the terms or timeline currently contemplated, or at all.
- We are a clinical stage biopharmaceutical company with a limited operating history and no products approved for commercial sale, and have incurred substantial losses since our inception and anticipate incurring substantial and increasing losses for the foreseeable future.
- Enrollment and retention of participants in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, including difficulties in identifying patients, the availability of competitive products and significant competition for recruiting participants in clinical trials.
- We will require substantial additional financing to achieve our goals, and failure to obtain additional capital when needed, or on acceptable terms to us, could cause us to delay, limit, reduce or terminate our product development or future commercialization efforts.
- Preclinical and clinical development involves a lengthy and expensive process, with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates.
- Our clinical trials may reveal serious adverse events (“SAEs”) and significant adverse events (“AEs”) and may result in a safety or tolerability profile that could delay or prevent regulatory approval or market acceptance of ESK-001, A-005 or any future product candidates.
- We face competition from entities that have made substantial investments into the rapid development of competitor treatments for immunological indications, including large and specialty pharmaceutical and biotechnology companies, many of which already have approved therapies and/or candidates under development in our current indications.
- Our business is highly dependent on the success of our most advanced product candidate, ESK-001, and we cannot guarantee that ESK-001 will successfully complete development, receive regulatory approval or be successfully commercialized. If we are unable to develop, receive regulatory approval for and ultimately successfully commercialize our product candidates, or if we experience significant delays in doing so, our business will be materially harmed.
- The regulatory approval processes of the U.S Food and Drug Administration (“FDA”) and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.
- We are dependent on the services of our management team and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.

- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates and any future product candidates we may develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, and our ability to successfully develop and commercialize our product candidates may be adversely affected.
- We cannot ensure that patent rights relating to inventions described and claimed in our or any future licensors' pending patent applications will issue or that patents based on our or any future licensors' patent applications will not be challenged and rendered invalid and/or unenforceable.
- We may form or seek collaborations or strategic alliances or enter into licensing arrangements in the future, and not realize the benefits of, such alliances or licensing arrangements.
- We may have conflicts with any potential future licensors or collaborators that could delay or prevent the development or commercialization of our product candidates.
- Even if we receive regulatory approval for our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal. We may also be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.
- As a result of our history of losses and negative cash flows from operations, our consolidated financial statements contain a statement regarding a substantial doubt about our ability to continue as a going concern.

PART I

Item 1. Business

Overview

Our mission is to significantly improve the lives of patients by replacing broad immunosuppression with targeted therapies. Our name, Alumis, captures our mission to enlighten immunology, and is inspired by the words “allumer”—French for illuminate—and “immunis”—Latin for the immune system.

We are a clinical stage biopharmaceutical company with an initial focus on developing our two Tyrosine Kinase 2 (“TYK2”) inhibitors: ESK-001, a second-generation inhibitor that we are developing to maximize target inhibition and optimize tolerability, and A-005, a central nervous system (“CNS”) penetrant molecule. ESK-001 has demonstrated significant therapeutic effect in our Phase 2 program in patients with PsO, which we define as moderate-to-severe plaque psoriasis (“PsO”), and is currently being evaluated in an additional Phase 2 clinical trial in patients with systemic lupus erythematosus (“SLE”), for which we expect to report results in 2026. With the favorable results in our Phase 2 clinical trial in PsO, we have initiated our Phase 3 ONWARD clinical program, which consists of two parallel Phase 3 clinical trials of ESK-001 in this indication and for which we expect to report topline results in the first quarter of 2026. These parallel Phase 3 clinical trials also include one long-term extension (“LTE”) study, ONWARD3. In addition, the open-label extension (“OLE”) of our Phase 2 clinical trial in PsO remains ongoing. TYK2 genetic mutations are associated with a strong protective effect in multiple sclerosis (“MS”), motivating us to develop our second product candidate, A-005, as a CNS-penetrant, allosteric TYK2 inhibitor for neuroinflammatory and neurodegenerative diseases. In April 2024, we initiated our Phase 1 program of A-005 in healthy volunteers and reported initial results in December 2024.

We utilize our proprietary precision data analytics platform, biological insights and team of experienced research and development experts to deepen our understanding of disease pathologies, accelerate research and development and increase the probability of clinical success. Our collective insights informed our selection of TYK2 as the target for our two lead programs. Beyond TYK2, our proprietary precision data analytics platform and drug discovery expertise have led to the identification of additional preclinical programs that exemplify our precision approach.

We recognize that patients living with immune-mediated diseases need alternatives to currently available therapies. Despite recent advances and innovations in the treatment of immune-mediated diseases, many patients continue to suffer, cycling through currently approved therapies while looking for a solution that alleviates the debilitating impact of their disease without life-limiting side effects.

Addressing the needs of these patients is why we exist. We are pioneering a precision approach that leverages insights derived from powerful data analytics to select the right target, right molecule, right indication, right patient, right endpoint and right combination to dramatically improve patient outcomes. We believe that combining our insights with an integrated approach to drug development will produce the next generation of treatments to address immune dysfunction.

Proposed Merger with ACELYRIN

On February 6, 2025, we entered into an Agreement and Plan of Merger (the “Merger Agreement”) with ACELYRIN, Inc., a Delaware corporation (“ACELYRIN”), and Arrow Merger Sub, Inc., a Delaware corporation and our direct wholly owned subsidiary (“Merger Sub”). Under the terms of the Merger Agreement, Merger Sub will merge with and into ACELYRIN, with ACELYRIN continuing as our direct wholly owned subsidiary (the “Merger”). The Merger Agreement was approved by the disinterested directors on our board of directors and the board of directors of ACELYRIN and is subject to stockholder approval by the stockholders of each company and satisfaction or waiver of other closing conditions.

In connection with the Merger, all of the issued and outstanding shares of common stock of ACELYRIN, par value \$0.00001 per share, will be cancelled and converted into the right to receive 0.4274 shares of our voting common stock, without interest (the number of shares of our common stock in exchange for each share of ACELYRIN common stock, the “Exchange Ratio”) and, if applicable, cash in lieu of fractional shares, subject to any applicable withholding.

Consummation of the Merger is subject to certain closing conditions, including the absence of any law or judgment that restrains, enjoins or otherwise prohibits consummation of the Merger, the effectiveness of a registration statement on Form S-4 to be filed by us with the Securities and Exchange Commission (the “SEC”), the adoption of the Merger Agreement by the holders of a majority of the outstanding shares of ACELYRIN common stock at ACELYRIN’s stockholders’ meeting and the approval of the share issuance by the holders of a majority of votes of the our common stock cast at our stockholders’ meeting.

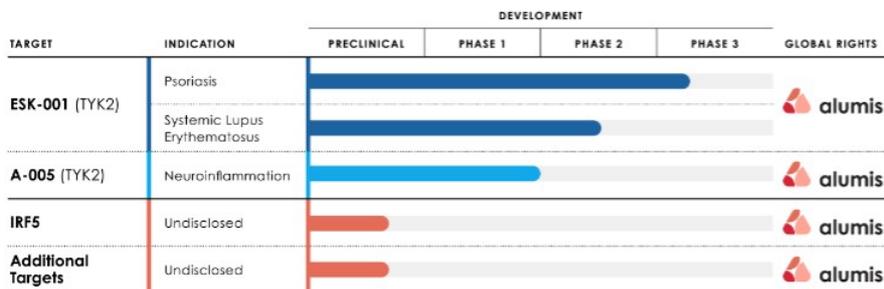
The Merger Agreement contains certain termination rights for both us and ACELYRIN, including the right of either party to terminate the Merger Agreement if the transactions have not been consummated prior to July 7, 2025. We or ACELYRIN will pay a termination fee of \$10.0 million or \$10.0 million, respectively, under certain circumstances, including termination to accept and enter into a definitive agreement with respect to a superior proposal.

Immediately following the Merger, our pre-Merger equityholders are expected to collectively own approximately 55% of the shares of the combined company and the pre-Merger equityholders of ACELYRIN as of immediately prior to the Merger are expected to collectively own approximately 45% of the combined company, in each case, calculated on a fully diluted basis as of January 31, 2025.

Our Product Candidates and Pipeline

We are building a pipeline of molecules with the potential to address a broad range of immune-mediated diseases as monotherapy or combination therapies. Within our TYK2 franchise, we are developing our most advanced product candidate, ESK-001, an allosteric TYK2 inhibitor for the treatment of PsO and SLE. We are developing our second TYK2 product candidate, A-005, as a CNS-penetrant allosteric TYK2 inhibitor, to offer the therapeutic benefit of TYK2 inhibition within the CNS for a broad range of neuroinflammatory and neurodegenerative diseases, and are pursuing MS as its initial indication.

The following chart summarizes the status of our current pipeline.



Our Strategy

Our mission is to significantly improve the lives of patients by replacing broad immunosuppression with targeted therapies. As our driving principle, we are using our precision approach focused on the important drivers of immune dysfunction. We use our key insights to pursue our mission of significantly improving outcomes for patients. We select drug targets that have been previously validated by strong human genetic evidence and human clinical data.

The core components of our business strategy include:

- **Maximize the opportunity presented by ESK-001’s differentiated pharmacological profile and breadth of potential indications.** We believe that ESK-001 is a foundational asset that exemplifies our approach. Genetic and biologic data generated to date highlight the important role of TYK2 inhibition across multiple diseases where we have current clinical programs (PsO and SLE) and future clinical ambitions. We intend to expand clinical

development of ESK-001 to additional therapeutic areas and indications where TYK2 inhibition and our differentiated profile have the potential to deliver significant improvements for patients.

- **Expand our TYK2 franchise with A-005, our allosteric TYK2 inhibitor selected to penetrate the CNS to treat neuroinflammation.** There is strong biological rationale for the involvement of TYK2 in neuroinflammatory and neurodegenerative diseases, as well as compelling genetic evidence for the role of TYK2 in MS. As a result, we believe TYK2 inhibition has potential utility in various neuroinflammatory and neurodegenerative diseases, including MS, Alzheimer’s disease, amyotrophic lateral sclerosis (“ALS”), optic neuritis, neuromyelitis optica and Parkinson’s disease.
- **Discover and advance earlier-stage product candidates into clinical development.** We intend to expand our pipeline of clinical-stage product candidates by identifying and developing earlier-stage assets. Utilizing our precision approach to address immune dysfunction, we have selected multiple additional targets to date, including interferon regulatory factor 5 (“IRF5”), across indications that are in various stages of development, from lead identification to lead optimization. These targets may enable development in a broad range of indications, either as a monotherapy or using a combination therapy approach with our TYK2 product candidate franchise.
- **Leverage our precision approach to increase speed of development, probability of success and precision of therapy.** We leverage our proprietary precision data analytics platform that integrates key genetic and translational insights, with the aim to design efficient and effective development paths at every stage of our pipeline. We believe this approach can bring forth transformative medications by following the science to inform the right target, right molecule, right indication, right patient, right endpoint and right combinations.
- **Evaluate strategic collaborations to maximize the global impact of our product candidates.** We plan to strategically evaluate potential partnerships to maximize the value of our lead programs and broader portfolio. We believe that our product candidates, indications, clinical data and data analytics make our company an attractive partner. Given our scientific expertise and significant therapeutic depth, and the broad addressable populations of our product candidates, the right partner could help us expand the breadth of indications we pursue and increase our commercial reach. For example, in February 2025, we announced the Merger. If we are successful in consummating the Merger, we expect to have the financial flexibility and runway to advance an expanded late-stage pipeline.

Immune Dysfunction Overview

The immune system is a highly regulated and balanced system that has evolved to protect us from infection, recognize and neutralize harmful agents from the environment and fight disease. Dysfunctional immune responses, whether directed towards self or non-self or through unbalanced activation or regulation, can lead to inflammation, allergy, autoimmunity and development of chronic immune-mediated diseases. We are building immune insights from patient samples, incorporating genetic, genomic and proteomic learnings, and translating preclinical findings in an effort to therapeutically target dysfunctional immune mechanisms to improve outcomes for patients with immune-mediated diseases.

Role of TYK2 in Immunology

TYK2 is an intracellular tyrosine kinase protein within the broader Janus kinase (“JAK”) family shown to play an essential role in mediating cytokine receptor signaling pathways in both innate and adaptive immunity. Cytokines are a group of proteins in the body that play an important role in boosting the immune system. TYK2 associates with a defined set of cytokine receptors expressed primarily on immune cells, such as IL-23, IL-12 and type I interferon (“IFN”) receptors, distinct from other JAK family members. TYK2 functions to relay signals into the cell through phosphorylation of signal transducing and activators of transcription (STATs), to initiate a cascade of protein-signaling interactions resulting in cytokine-responsive gene transcription and cell activation, which drives downstream immune responses including Th17, IL-17 pathways, and type I IFN responsive genes that are known drivers of inflammation and immune mediated disease. Therapeutic inhibition of TYK2 and associated cytokine pathways, in particular IL-23/IL-17 and type I IFN, have been broadly validated to address immune dysfunction in immune-mediated diseases, such as psoriasis, psoriatic arthritis and

SLE. TYK2 is expressed in circulating and tissue-resident immune cells, and is also active in CNS-resident immune cells, such as microglia, which are thought to play a key role in neuroinflammation.

Human genetic studies of TYK2 strongly validated it as a therapeutic target. An identified loss-of-function mutation (“P1104A”) in the TYK2 gene, present in approximately 3% to 5% of European populations, is protective against an array of immune-mediated disorders, including SLE, psoriasis, sarcoidosis, psoriatic arthritis, inflammatory bowel disease and neuroinflammatory and neurodegenerative conditions, such as MS. Importantly, this TYK2 variant does not appear to significantly increase susceptibility to serious infections. We believe that TYK2 inhibition as a targeted therapy may have an improved risk to benefit profile as compared to broad immune suppression.

TYK2 inhibition represents a breadth of opportunity, and there have been or are ongoing clinical trials of TYK2 inhibitors in multiple indications such as psoriatic arthritis, SLE, cutaneous lupus, alopecia areata, Sjogren’s disease, vitiligo, Crohn’s disease and ulcerative colitis.

Our TYK2 Franchise

ESK-001: Our Allosteric TYK2 Inhibitor

ESK-001 is a potent, highly selective, allosteric TYK2 inhibitor.

Key Differentiating Features

We believe ESK-001 is differentiated from first-generation TYK2 inhibitors for the following reasons:

- **Intrinsic Selectivity and Preclinical Pharmacology.** Due to ESK-001’s design as an allosteric inhibitor, the molecule is both potent and intrinsically selective for TYK2 over other protein kinases, including the related JAK family members. No JAK-related pharmacology has been observed with ESK-001 to date.
- **Optimized Molecular Properties and PK.** At the core of ESK-001’s differentiation from other clinical-stage allosteric inhibitors of TYK2 are its physicochemical properties that we believe impart highly desirable drug-like features. ESK-001 is highly permeable with low efflux resulting in high and rapid systemic absorption and favorable tissue distribution *in vivo*. These properties result in its highly predictable, linear PK profile in humans with low variability. In addition, ESK-001 has a desirable half-life in humans of approximately 8 to 12 hours and we have not observed any concerns for drug-drug interactions with other therapies.
- **Maximal Target Inhibition.** ESK-001 demonstrated a robust and predictable PK/PD relationship in Phase 1 studies, enabling the identification of a dose level that achieved maximal TYK2 inhibition for 24 hours a day to take into Phase 2 clinical trials. We define maximal inhibition as reaching the plateau of biological inhibition in the assay readout with no further impact seen with higher drug concentrations. At the 40 mg BID dose, maximal TYK2 inhibition was confirmed in healthy volunteer and PsO patient blood samples by RNA-seq analysis, and a return to non-lesional baseline levels of TYK2 pathway (including IFN signature, IL-23, IL-17) and PsO-relevant disease biomarkers was confirmed in PsO patient skin biopsies.
- **Clinical Tolerability.** There have been no clinically limiting findings across our clinical trials to date that prevent ESK-001 from being dosed to achieve maximal target inhibition. In contrast to what has been reported with first-generation allosteric TYK2 inhibitors, skin rashes have been observed at much lower frequency with ESK-001 to date, even at very high and sustained levels of target inhibition, suggesting that skin toxicities may not be an on-target, class effect of TYK2 inhibitors.

Strategic Indication Selection

TYK2-mediated cytokine signaling is involved in a broad range of immune-mediated diseases. TYK2 loss-of-function mutations have been shown to be protective for several conditions including psoriasis, psoriatic arthritis, Crohn’s disease,

ulcerative colitis and MS. Therefore, ESK-001 has the potential to provide benefit in a large number of indications. We have selected PsO and SLE as our initial indications.

Combination Potential

Despite significant advances in the treatment of immune-mediated disease, in many diseases, only a minority of patients achieve disease remission or nearly complete response with current therapies. Because of the complexity, overlap and redundancy of inflammatory pathways, combination approaches targeting complementary pathways may be needed to achieve high-hurdle endpoints such as remission. We believe that ESK-001's pharmacological properties, including its lack of drug-drug interaction potential and its clinical profile, positions it well as a partner for future combination therapies.

Development

ESK-001 is currently being evaluated in two parallel Phase 3 clinical trials in PsO as well as in a Phase 2b clinical trial in SLE.

ESK-001 for the Treatment of Moderate-to-Severe Plaque Psoriasis (PsO)

Psoriasis is a chronic immune-mediated skin disease characterized by abnormal epidermal growth, usually presenting as red, scaly patches, papules or plaques (plaque psoriasis). Patients with psoriasis are also at increased risk of developing other co-morbid conditions, such as cardiovascular disease, obesity, insulin resistance, uveitis, arthritis and thyroid dysfunction. According to the World Health Organization, psoriasis significantly impacts quality of life—physical and emotional challenges of disfigurement, low self-esteem, loss of productivity and depression.

ESK-001 has advanced to Phase 3 development in PsO. In March 2024, we announced positive data from our randomized, double-blind, placebo-controlled Phase 2 clinical trial in patients with PsO (“Phase 2 STRIDE trial”). Our Phase 2 STRIDE trial met its primary endpoint, the proportion of patients achieving a 75% improvement in the Psoriasis Area and Severity Index (“PASI 75”) at week 12 compared to placebo, and key secondary efficacy endpoints at all clinically relevant doses tested. Clear dose-dependent responses were observed with maximal TYK2 inhibition achieved, and highest clinical response rates observed, at the highest dose of 40 mg twice daily. ESK-001 was found to be generally well tolerated at all dose levels. Upon completion of the Phase 2 STRIDE trial, patients were eligible to be enrolled in an OLE study evaluating two ESK-001 doses (40 mg once daily and 40 mg twice daily), which we designed to evaluate the safety and efficacy of long-term treatment with ESK-001 in patients with PsO. The OLE study remains ongoing and, at Week 40, all participants on the 40 mg once daily cohort transitioned to the 40 mg twice daily dose. In September 2024, we announced positive 28-week data from the OLE, which showed dose-dependent sustained increases in Psoriasis Area and Severity Index (“PASI”) endpoint responses observed over time, with the majority of patients achieving PASI 75, the primary endpoint, at the highest dose of 40 mg twice daily. ESK-001 was generally well-tolerated in the OLE Week 28 data. In March 2025, we announced positive 52-week data from the OLE, which demonstrated sustained PASI 90 and increased PASI 100 response rates in the 40 mg twice daily cohort. ESK-001 was generally well-tolerated in the OLE Week 52 data. See “—Safety Profile of ESK-001” below for further information.

With the favorable results in our Phase 2 STRIDE trial in PsO, we have initiated our Phase 3 ONWARD clinical program, which consists of two parallel global Phase 3, multi-center, randomized, double-blind placebo-controlled clinical trials, ONWARD1 and ONWARD2, designed to evaluate the efficacy and safety of ESK-001 in this indication. These parallel Phase 3 clinical trials also include one LTE study, ONWARD3.

ESK-001 for the Treatment of Systemic Lupus Erythematosus (SLE)

SLE is a chronic autoimmune disease predominantly affecting women at childbearing age. Clinical manifestations are highly heterogeneous, and the disease typically waxes and wanes, with flares and periods of relative remission. Certain loss-of-function variants of TYK2 significantly decrease the risk of SLE. While mortality in SLE has decreased since the mid-20th century as a result of improved treatments, the disease remains associated with increased disability and loss of social and occupational functioning and high utilization of health care resources.

We are currently conducting LUMUS, a Phase 2b, 48-week, global, placebo-controlled, double-blind, randomized, clinical trial evaluating ESK-001 in patients with moderate-to-severe active SLE, in the United States, Europe, the United Kingdom (“UK”), Latin America and Asia-Pacific (“APAC”) countries. The primary endpoint in Part A of such trial is BILAG-Based Composite Lupus Assessment response (a validated composite measure of lupus disease activity) at Week 48. Eligible patients may enroll in Part B (an OLE) or participate in a four-week follow-up period.

Safety Profile of ESK-001

ESK-001 has been administered to more than 800 participants and in some cases administered for up to two years. ESK-001 has been generally well-tolerated in our Phase 2 STRIDE and OLE clinical trials to date, with the majority of AEs observed in such clinical trials having been graded mild-to-moderate in severity. As of December 31, 2024, the most common AEs reported by patients across active (ESK-001) trial arms were headaches, upper respiratory tract infections and nasopharyngitis, and the most common AEs deemed related to study drug by the principal investigator included headaches, upper respiratory tract infections, nasopharyngitis, rash and nausea. The safety profile of ESK-001 continues to be evaluated in our ongoing Phase 2 OLE and Phase 3 trials.

ESK-001 is an allosteric inhibitor of TYK2. TYK2 is an intracellular tyrosine kinase protein shown to play an essential role in mediating cytokine receptor signaling pathways in both innate and adaptive immunity. Cytokines are a group of proteins in the body that play an important role in boosting the immune system. Other TYK2 inhibitors, such as deucravacitinib (marketed as Sotyktu which is approved for the treatment of adults with PsO), have shown AEs such as hypersensitivity reactions, infections, tuberculosis, malignancy and rhabdomyolysis. The label for deucravacitinib includes a warning concerning the potential for JAK-related adverse events, such as cardiovascular and thrombotic events. Given our similar mechanism of action, we closely monitor and characterize these potential safety risks in our clinical studies. We have observed, and expect to continue to observe that additional AEs and SAEs, consistent with known side effects of TYK2 inhibition may emerge in our ongoing and future clinical trials of ESK-001, and we have also observed and expect to continue to observe trial participant withdrawals or discontinuations due to AEs. As of December 31, 2024, four SAEs (one serious infection, one arthritis and two malignancy cases) were reported in the STRIDE OLE trial and considered related to ESK-001 treatment by the principal investigator. We observed these cases of serious infection and malignancy were reported in participants with relevant comorbidities and/or (in one malignancy case) relevant family history.

A-005: Our CNS-Penetrant Allosteric TYK2 Inhibitor

The second clinical product candidate in our TYK2 franchise, A-005, is a highly differentiated, CNS-penetrant, allosteric TYK2 inhibitor that has potential applications in multiple sclerosis and other neurological diseases. A loss-of-function mutation in the TYK2 gene has been shown by our proprietary genetic data set as well as scientific literature, to reduce the risk of developing MS.

Role of TYK2 in Neuroinflammatory and Neurodegenerative Diseases

TYK2 pathways are active in CNS-resident immune cells and may play a localized role in the CNS contributing to the pathology of several CNS inflammatory disorders, including MS. Genome-wide association studies have shown the loss-of-function TYK2 genetic variant, P1104A, has a protective effect for the development of MS. An additional missense variant in TYK2, Rs35018800, has the largest effect on MS risk of any variant outside the MHC/HLA region discovered to date. In addition to its genetic association with MS, TYK2 is known to be expressed and functionally active in CNS-resident microglia. Microglia express IL-23 and interferon receptors and IL-23/IL-12 cytokines have been shown to localize to MS lesions. Activated microglia are associated with disease worsening in MS, and TYK2 inhibitors with adequate CNS exposure may provide an opportunity to target neuroinflammation and neurodegeneration. We believe TYK2 inhibition has the potential to treat the neuroinflammatory component of other neurodegenerative diseases where activated microglia and/or TYK2 proinflammatory cytokines including interferon are implicated such as Alzheimer’s disease, ALS, optic neuritis, neuromyelitis optica, and Parkinson’s disease.

Development

A-005 for the Treatment of Multiple Sclerosis

MS is a chronic immune-mediated disease of the central nervous system. This condition causes a wide range of physical and cognitive challenges for those afflicted, often resulting in neurological symptoms and disabilities. Despite available treatments to manage symptoms and slow disease progression, treatments are limited for progressive disease and a definitive cure remains elusive. Agents directly targeting the CNS pathology and CNS resident cells, including activated microglia, are of increasing interest as these are thought to impact progressive neurological impairment. The unmet need lies in finding safe and more effective targeted therapies that can halt or reverse the disease progression, alleviating the burden on patients and their families and improving their overall quality of life.

In December 2024, we announced positive data from a Phase 1 clinical trial evaluating the safety, tolerability and PK of single- and multiple-ascending doses of A-005 in healthy participants. In the clinical trial, A-005 was well tolerated with no SAEs reported.

Our Discovery Programs

We are building a pipeline of molecules with the potential to address a broad range of immune-mediated diseases. We pursue drug targets that have been previously validated by strong human genetic evidence or human clinical data. Our drug discovery efforts for our selected targets take advantage of structure-guided approaches built from public or proprietary crystallographic structures to enable use of advanced computational methods. These approaches enable optimization of traditional protein modulators, protein degraders, and targeted covalent inhibitors as appropriate. In addition, we have chosen targets that could be complementary for use in combination with our existing TYK2 franchise and to each other.

For example, interferon regulatory factor 5 (“IRF5”) is a transcription factor that mediates signaling of several cytokines including type I IFN, IL-6, IL-12, IL-23, and TNF. It is a genetically supported target across multiple immune indications with known functional roles in both innate and adaptive immunity. IRF5 has been implicated in macrophage polarization, cell growth regulation, and apoptosis. It acts on innate immune responses via recognition of upstream self-nucleic acid-containing immune complexes and pathogens by toll like receptors (“TLR”), specifically: TLR7, TLR8 and TLR9 in the endosome via MyD88. Translocation of IRF5 to the nucleus following phosphorylation by IKK β is critical to the pathogenesis of many immune mediated diseases. Genome-wide association studies have identified several functional genetic variants in IRF5 that predispose patients to immune-mediated diseases including, but not limited to SLE, systemic sclerosis, and primary sclerosing cholangitis.

We are actively engaged in lead generation activities to identify small molecules that can precisely bind and block IRF5 function. These efforts are aided by our proprietary crystal structure of our compounds bound to IRF5, which enables computational approaches to optimize binders for either IRF5 inhibition or degradation. We have developed several proprietary assays including a biochemical dimerization assay that has been used in conjunction with high-throughput screening to identify leads. In addition, we have applied an orthogonal method to identify small-molecule binders that may target allosteric pockets providing inhibition directly or as a component in a proteolysis-targeting chimera. We will pursue multiple mechanisms of inhibition and use our extensive pharmacology expertise to guide the final selection of clinical candidates.

Foresite Labs Services Agreement

Foresite Labs, LLC (“Foresite Labs”) was an original stockholder in, and actively involved in our incubation. We and Foresite Labs have had an ongoing services agreement since our inception, with Foresite Labs originally providing incubation services, development assistance and oversight, and data analytics services; currently, Foresite Labs provides data analytics services related to our TYK2 franchise, our discovery programs and to our business development activities. The original Services Agreement between us and Foresite Labs was entered into in January 2021, was amended and restated in August 2021, was amended and restated for a second time in December 2023, and expires in December 2026, unless terminated earlier by the parties. Work under the Services Agreement is memorialized in a series of Statements of

Work and we pay Foresite Labs for the estimated costs of its services in advance on a quarterly basis, with a true-up to actuals at the end of each quarter.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including by seeking, maintaining, enforcing and defending patent rights. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology, assays and product candidates, and may in the future rely on in-licensing opportunities, to develop, strengthen and maintain our proprietary position in our field. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to obtain and maintain any future licenses to use intellectual property owned by third parties; and to defend and enforce our proprietary rights, including our patent rights.

As of December 31, 2024, our solely owned patent portfolio included four issued U.S. patents, over five pending U.S. provisional patent applications, over five pending non-provisional U.S. patent applications, over five granted foreign patents, which includes a granted European patent validated in over 35 countries, over 80 pending foreign patent applications, and five pending Patent Cooperation Treaty (“PCT”) patent applications.

ESK-001 and A-005

In regard to ESK-001 and A-005, we own one patent family with claims directed to composition of matter and methods of use that includes four issued U.S. patents, one pending U.S. patent application, over five granted foreign patents in Europe (validated in over 35 countries), and certain other countries, and over 10 foreign patent applications pending in various jurisdictions, such as Europe, Canada, China, Australia, Japan and India. Not accounting for any patent term adjustment or extensions or terminal disclaimers, and assuming that all applicable annuity and/or maintenance fees are paid timely, the issued patents, and, if granted, the pending patent applications in this family, are expected to expire in 2039.

We also own three patent families with claims directed to crystalline and salt forms of ESK-001, which includes two pending PCT applications, one pending U.S. application, and over 20 foreign patent applications pending in various jurisdictions such as Europe, Canada, China, Australia and Japan. Not accounting for any patent term adjustment or extension and assuming that all applicable annuity and/or maintenance fees are paid timely, the patent applications, if issued, and any patent applications claiming the benefit of these PCT applications, if issued, will be expected to expire in 2043.

We own one patent family with claims directed to methods of treating a TYK2-mediated disease using ESK-001, that includes a pending U.S. application and over 10 foreign applications pending in various jurisdictions such as Europe, Brazil, Canada, China, Australia and Japan. Not accounting for any patent term adjustment or extension and assuming that all applicable annuity and/or maintenance fees are paid timely, any patent applications, if issued, will be expected to expire in 2043.

We own two pending PCT applications and one pending U.S. provisional patent application that disclose and/or contain claims directed to methods of treating various diseases with ESK-001. Not accounting for any patent term adjustment or extension and assuming that all annuity and/or maintenance fees are paid timely, any patent applications claiming the benefit of the PCT applications, or patent applications claiming priority to the PCT applications or the provisional patent application, if issued, will be expected to expire between 2044 and 2045.

We own three pending U.S. provisional patent applications with claims directed to crystalline and salt forms of A-005, one pending U.S. provisional patent application with claims directed to processes for making ESK-001, and one pending U.S. provisional patent application with claims directed to formulations of ESK-001. Not accounting for any patent term adjustment or extension and assuming that all applicable annuity and/or maintenance fees are paid timely, any patent applications claiming priority to the provisional applications, if issued, will be expected to expire in 2045.

We continue to assess the extent to which we may seek additional patent protection for aspects of our product engine. The term of individual patents depends upon the date of filing of the patent application, date of patent issuance and the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of the first non-provisional application to which priority is claimed. Outside of the United States, the duration of patents varies in accordance with applicable local law, but typically is also 20 years from the earliest non-provisional filing date. In the United States, patent term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office (“USPTO”) in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. Moreover, in context of approved products, there may be other additional exclusivity for the patents covering such approved product. In the United States, the term of a patent that covers an FDA-approved drug may also be eligible for a patent term extension of up to five years under the Hatch-Waxman Act, which is designed to compensate for the patent term lost during the FDA regulatory review process. The length of the patent term extension is calculated based on the length of time it takes for regulatory review. A patent term extension under the Hatch-Waxman Act cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be restored and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Moreover, a patent can only be restored once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug.

We intend to pursue, in the normal course of business and when possible, composition, method of use, process, dosing and formulation patent protection for the product candidates we develop and commercialize. We may also pursue patent protection with respect to manufacturing and immunotherapy development processes and technology. When available to expand market exclusivity, we intend to strategically obtain or license additional intellectual property related to current or contemplated product candidates.

In some instances, we submit patent applications directly to the USPTO as provisional patent applications. Corresponding non-provisional patent applications must be filed within 12 months after the provisional application filing date. The corresponding non-provisional application may be entitled to the benefit of the earlier provisional application filing date(s), and the patent term of the finally issued patent is calculated from the later non-provisional application filing date. Provisional applications for patents were designed to provide a lower-cost first patent filing in the United States. This system allows us to obtain an earlier priority date, add material to the patent application(s) during the priority period, obtain a later start to the patent term and to delay prosecution costs.

The PCT system allows a single application to be filed within 12 months of the original priority date of the patent application, and to designate all of the PCT member states in which national or regional patent applications can later be pursued based on the international patent application filed under the PCT. The PCT searching authority performs a patentability search and issues a non-binding patentability opinion which can be used to evaluate the chances of success for the national or regional applications prior to having to incur the filing fees and prosecution costs. Although a PCT application does not issue as a patent, it allows the applicant to seek protection in any of the member states through national/regional-phase applications. At the end of the period of two and a half years from the first priority date of the patent application, separate patent applications can be pursued in any of the PCT member states either by direct national filing or, in some cases by filing through a regional patent organization, such as the European Patent Organisation. The PCT system delays expenses, allows a limited evaluation of the chances of success for national/regional patent applications and enables substantial savings where applications are abandoned within the first two and a half years of filing. We intend to file U.S. nonprovisional applications and PCT applications that claim the benefit of the priority date of earlier filed provisional applications, when applicable.

For all patent applications, we determine claiming strategy on a case-by-case basis. Advice of counsel, country-specific patent laws and our business model and needs are always considered. We may file patents containing claims for protection of all useful applications of our proprietary product candidates, as well as all new applications and/or uses we discover for existing product candidates, assuming these are strategically valuable. We continuously reassess the number and type of patent applications in our portfolio, as well as the pending and issued patent claims, to help ensure that maximum coverage and value are obtained for our processes, and compositions, given existing patent office rules and regulations. Further,

claims may be modified during patent prosecution, to the extent allowed, to meet our intellectual property and business needs.

There can be no assurance that we will be able to obtain, maintain, enforce and defend all patents and other intellectual property rights necessary to conduct our business. The patents that issue from our patent applications or any that we may in-license in the future, if any, may be challenged by third parties, may not effectively prevent third parties from commercializing competitive technologies or may not otherwise provide us with a competitive advantage.

We may also rely on trade secrets relating to our product candidates and technology, and seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. However, trade secrets are difficult to protect and may provide us with only limited protection. It is our policy and practice to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us, and for employees and consultants to enter into invention assignment agreements with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Where applicable, the agreements provide that all inventions to which the individual contributed as an inventor shall be assigned to us, and as such, will become our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

For more information regarding the risks related to our intellectual property, see Item 1A. "Risk Factors — Risks Related to Intellectual Property."

Sales and Marketing

Given our stage of development, we have not yet established a full commercial organization or distribution capabilities. We have stage-appropriate commercial capabilities and we intend to build a commercial infrastructure to support sales of any approved products. We also intend to continue evaluating opportunities to work with partners that enhance our capabilities with respect to the development and commercialization of ESK-001 and A-005, if approved. In addition, we intend to commercialize our product candidates, if approved, in key markets in the United States, the European Union ("EU") and APAC, either alone or with partners in order to maximize the worldwide commercial potential of our programs.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for clinical testing, as well as for manufacture of any products that we may commercialize, if approved. To date, we have obtained active pharmaceutical ingredients ("API") for ESK-001 and A-005 for our preclinical and clinical testing from different third-party API manufacturers and bulk drug product from other third-party manufacturers. We obtain our preclinical and clinical supplies from these manufacturers on a purchase order basis and currently do not have long-term supply arrangements in place. Our principal suppliers of critical raw materials are located in India and in Taiwan. We are in the process of implementing a redundant supply chain for ESK-001 API, drug product and critical raw material. For all our product candidates, we intend to identify and qualify redundant manufacturers to provide the API and drug product and prior to submission of the NDA to the FDA and/or a marketing authorization application to the European Medicines Agency ("EMA") and/or other health authorities. ESK-001 and A-005 are compounds of low molecular weight, generally called small molecules. ESK-001 can be manufactured in reliable and reproducible processes from readily available starting materials. A-005 has been produced in small quantities to support our preclinical studies and is currently being manufactured at larger quantities for clinical testing. The chemistries for ESK-001 and A-005 are amenable to scale-up and do not require unusual equipment in the manufacturing process. Additional contract manufacturers are used to package, label, and distribute investigational drug products. This strategy allows us to maintain a more efficient infrastructure, avoid depending on our own manufacturing facility and equipment while simultaneously enabling us to focus our expertise on developing our products. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies and generic drug companies. Many of our potential competitors have greater financial and technical human resources than we do, as well as equal or greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our potential competitors may be more successful than us in achieving regulatory approvals and commercializing their drugs. We anticipate that we will face intense and increasing competition from existing, approved drugs, as well as new drugs entering the market and emerging technologies that become available. Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates non-competitive or obsolete.

We believe the key competitive factors that will affect the development and commercial success of our product candidates, if approved, will be efficacy, safety, tolerability profile, convenience of dosing, price and coverage by governmental and third-party payors.

We are currently developing ESK-001 for the treatment of PsO and SLE, with multiple other potential indications to follow. Other emerging and established life sciences companies have been focused on similar therapeutics. If approved, ESK-001 would compete with several currently approved or late-stage oral clinical therapeutics in each such indication as well as other drugs used to treat such patients.

Our second TYK2 product candidate, A-005, is a highly differentiated CNS-penetrant allosteric TYK2 inhibitor that has a potential application in MS and other neuroinflammatory diseases. In MS, there are a large number of therapies available for the treatment of relapsing forms of MS, including interferon beta regulators, monoclonal antibodies, synthetic immunomodulatory drugs, and S1P receptor modulators.

Coverage and Reimbursement

Successful sales of approved drug products in the U.S. market will depend, in part, on the extent to which such drugs will be covered by third-party payors, such as government health programs or private health insurance (including managed care plans). Patients who are provided with prescriptions as part of their medical treatment generally rely on such third-party payors to reimburse all or part of the costs associated with their prescriptions and therefore adequate coverage and reimbursement from such third-party payors are critical to new and ongoing product acceptance. Coverage and reimbursement policies for drug products can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for drug products among third-party payors in the United States. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time consuming and costly. Further, third-party payors are increasingly reducing reimbursements for medical drugs and services and implementing measures to control utilization of drugs (such as requiring prior authorization for coverage).

Additionally, the containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic drugs. Adoption or expansion of price controls and cost-containment measures could further limit manufacturers' net revenue and results. Decreases in third-party reimbursement for a manufacturer's drug products or a decision by a third-party payor to not cover its drug products could have a material adverse effect on the manufacturer's sales, results of operations and financial condition.

General legislative cost control measures may also affect reimbursement for drug products. Manufacturers that obtain approval to market a drug candidate in the United States may be subject to spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs and/or any significant taxes or fees.

Government Regulation

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

U.S. Drug Development Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA under the Federal Food, Drug, and Cosmetic Act (“FDCA”) and its implementing regulations. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies in accordance with Good Laboratory Practice regulations (“GLPs”) and other applicable regulations;
- submission to the FDA of an Investigational New Drug (“IND”) application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (“IRB”) or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice regulations (“GCPs”) to evaluate the safety and efficacy of the drug for its intended use;
- submission to the FDA of a New Drug Application (“NDA”);
- a determination by the FDA within 60 days of its receipt of the NDA to file the submission for review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice (“cGMP”) requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity, and of inspection of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Nonclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the nonclinical tests must comply with federal regulations and requirements, including GLPs, where applicable. The results of nonclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls (“CMC”), and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

Clinical trials involve the administration of the investigational drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCPs, which are standards meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters

to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an IRB for approval before a clinical trial commences at the relevant institution. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions on the conduct of the study.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy subjects or patients, the drug is tested to assess safety, dosage tolerance, metabolism, pharmacokinetics, pharmacological actions, side effects associated with drug exposure and, if possible, to gain early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population with the specified disease or conditions to evaluate the effectiveness of the drug for a particular indication, to determine optimal dose and regimen, and to identify common AEs and safety risks. If preliminary evidence of effectiveness and an acceptable safety profile is obtained in Phase 2 evaluations, Phase 3 trials are conducted. Phase 3 trials are undertaken to obtain additional information about clinical efficacy and safety in an expanded patient population, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug.

In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the safety and efficacy of a novel drug product. A single Phase 3 trial may be sufficient in rare instances, including (1) where the study is a large, multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (2) when the single trial is supported by confirmatory evidence.

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

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

U.S. Review and Approval Process

After completion of the required clinical testing, the sponsor prepares and submits an NDA to the FDA. FDA approval of the NDA is required before marketing and distribution of the product may begin in the United States. The NDA must include, among other information, the results of all nonclinical, clinical, and other testing along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, and proposed labeling. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee. Under an approved NDA, the applicant is also subject to an annual program fee. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be filed based on the FDA's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is filed, the FDA begins an in-depth review. Under the Prescription Drug User Fee Act, as amended ("PDUFA"), the FDA has agreed to certain performance goals in its review of NDAs. For new molecular entity ("NME") NDAs that are granted Standard

Review, the FDA's goal is to review and act on the NDA within ten months of the date the FDA files the application. For NME NDAs granted a Priority Review, the FDA's goal is to review the NDA within six months of the date the FDA files the application. The FDA may extend its PDUFA goal date for reviewing both standard and priority-review NDAs for three additional months to allow the FDA to consider certain late-submitted information or information intended to clarify information already provided in the NDA submission.

The FDA may also refer applications for novel drugs, as well as drugs that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation and a recommendation as to whether the NDA should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will generally inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve a drug unless the facility at which the drug is manufactured has a satisfactory cGMP compliance status.

After the FDA evaluates the NDA and completes any clinical and manufacturing site inspections, it issues either an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A complete response letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A complete response letter generally outlines the deficiencies in the NDA and may require substantial additional testing or information that must be provided in order for the FDA to reconsider the NDA for approval. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such NDA resubmissions in two or six months from the date of receipt, depending on the type of information included.

As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy (“REMS”) to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use (“ETASU”). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, the FDA may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy.

FDA Expedited Development and Review Programs

The FDA has a number of programs intended to expedite the development or review of a marketing application for an investigational drug product. For example, the Fast Track designation program is intended to expedite or facilitate the process for developing and reviewing drug products that meet certain criteria. Specifically, investigational drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. The sponsor of a Fast Track drug candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. With regard to a Fast Track drug candidate, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

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

Any drug product submitted to the FDA for approval, including a drug with a Fast Track designation or Breakthrough Therapy Designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as Priority Review. An NDA is eligible for Priority Review if the applicable drug is designed to treat a serious condition, and if approved, would provide a significant improvement in safety or efficacy compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an NDA for a drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review NDAs for NMEs with Priority Review designations within six months of the filing date as compared to ten months for Standard Review NDAs under its current PDUFA review goals.

Fast Track designation, Breakthrough Therapy designation, and Priority Review do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including investigational drugs, are required to register and disclose certain clinical trial information on ClinicalTrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is determined by the FDA to be safe and effective. The FDA may grant full or partial waivers or deferrals for submission of data. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or submit a request for approval of a pediatric formulation.

The Best Pharmaceuticals for Children Act (“BPCA”) provides NDA holders a six-month extension of any exclusivity—patent or nonpatent—for a drug if certain conditions are met. Conditions for exclusivity include the FDA’s determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a “written request” for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications or supplements to an approved application that propose a labeling change as a result of pediatric studies conducted pursuant to the BPCA are treated as priority applications or supplements, with all of the benefits that designation confers.

Post-Approval Requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, many changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval.

Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the FDA inspects manufacturing facilities to assess compliance with cGMP. Changes to the manufacturing process

are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMP.

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

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

The FDA strictly regulates marketing, labeling, advertising and promotion of drugs that are placed on the market. Advertising and promotion of drugs must be in compliance with the FDCA and its implementing regulations and only for the approved indications and in a manner consistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities.

Foreign Drug Development Processes

In addition to regulations in the United States, we are and will continue to be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials, authorization, and any commercial sales and distribution of our products. Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Many countries outside of the United States have a process similar to that in the United States that requires the submission of a clinical trial application (“CTA”) much like the IND prior to the commencement of human clinical trials.

Although in countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country in all cases, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our potential collaborators fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension, variation or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Clinical Trials in the EU

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. In the EU, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014 (the “CTR”), which entered into application on January 31, 2022, repealing and replacing the former Clinical Trials Directive 2001/20 (the “CTD”).

The CTR is intended to harmonize and streamline CTA, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase transparency. Specifically, the regulation, which is directly applicable in all EU member states, introduces a streamlined application procedure through a single-entry point, the “EU portal”; the Clinical Trials Information System (“CTIS”); a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is led by the competent authorities of a reference member state selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU member states. This assessment is then submitted to the competent authorities of all concerned member states in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and ethics committees in each concerned EU member state, i.e., all EU member states in which a clinical trial is to be conducted. Individual EU member states retain the power to authorize the conduct of clinical trials on their territory.

The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR.

Medicinal products used in clinical trials must be manufactured in accordance with the guidelines on GMP and in a GMP certified facility, which is subject to GMP inspections.

Review and Approval Process of Medicinal Products in the EU

In the EU, medicinal products can only be commercialized after a related marketing authorization (“MA”) has been granted. To obtain an MA for a medicinal product in the EU, an applicant must submit a Marketing Authorization Application (“MAA”), either in accordance with a centralized procedure administered by the EMA, or one of the procedures administered by the competent authorities of EU member states (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

A successful application in accordance with the centralized procedure results in the grant of a single MA by the European Commission that is valid throughout the EU. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) advanced therapy medicinal products (“ATMPs”), and (iv) products with a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval.

In accordance with the centralized procedure, the EMA’s Committee for Medicinal Products for Human Use (the “CHMP”), conducts the initial assessment of an application for authorization of a medicinal product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of variations or extensions to an existing MA. The maximum timeframe for the evaluation of an MAA under the centralized procedure is 210 days, excluding clock stops during which additional information or written or oral explanations are provided by the applicant in

response to questions of the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product that targets an unmet medical need is expected to be of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts a request for accelerated assessment, the time limit of 210 days will be reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU member state in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid MAA. The resulting assessment report is submitted to the concerned EU member states who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU 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 Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralized Procedures — Human ("CMDh") for review. The subsequent decision of the European Commission is binding on all EU member states.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU member state to apply for this authorization to be recognized by the competent authorities in other EU member states. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU member states of the MA granted in relation to a medicinal product by the competent authorities of other EU member states. The holder of a national MA may submit an application to the competent authority of an EU member state requesting that this authority recognize the MA delivered by the competent authority of another EU member state.

An MA has, in principle, an initial validity of five years. The MA 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 EU member state in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the Common Technical Document providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or the competent authorities of the EU member states may decide on justified grounds relating to pharmacovigilance, to proceed with one further five-year renewal period for the MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU member state within three years after authorization ceases to be valid (the so-called sunset clause) unless, in justified circumstances, authorization is extended.

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRiority MEDicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicinal products that target unmet medical needs. Eligible products must target conditions for which there is an unmet medical need; i.e., where there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicinal product will bring a major therapeutic advantage. The products must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. 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 potentially accelerated MAA assessment once a dossier has been submitted.

In the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization; (iii) the medicinal product fulfils an unmet medical need; and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the

fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and must be renewed annually until all related conditions have been fulfilled. Once any pending studies are provided, the conditional MA can be converted into a standard MA. However, if the conditions are not fulfilled within the timeframe set by the EMA and approved by the European Commission, the MA will cease to be renewed.

An MA may also be granted “under exceptional circumstances” where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. These circumstances may arise in particular when the intended indications are very rare and, in the state of scientific knowledge at that time, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Like a conditional MA, an MA granted in exceptional circumstances is reserved to medicinal products intended to be authorized for treatment of rare diseases or unmet medical needs for which the applicant does not hold a complete data set that is required for the grant of a standard MA. However, unlike the conditional MA, an applicant for authorization in exceptional circumstances is not subsequently required to provide the missing data. Although the MA “under exceptional circumstances” is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually, and the MA will be withdrawn if the risk-benefit ratio is no longer favorable.

Pediatric Development in the EU

In the EU, Regulation (EC) No 1901/2006 provides that all MAAs for new medicinal products must include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan (“PIP”) agreed with the EMA’s Pediatric Committee (“PDCO”). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the medicinal product for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures provided in the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU member states and study results are included in the product information, even when negative, the product is eligible for a six-month extension to the Supplementary Protection Certificate (“SPC”), if any is in effect at the time of authorization or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity.

Data and Market Exclusivity in the EU

The EU provides opportunities for data and market exclusivity related to MAs. Upon receipt of an MA, innovative medicinal products (i.e., reference products) are generally entitled to benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity, if granted, prevents generic and biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall ten-year period may, occasionally, be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU’s regulatory authorities to be a new chemical/biological entity, and products may not qualify for data exclusivity.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product. For such products, the results of appropriate preclinical or clinical trials must be provided in support of an application for MA. Guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product.

Manufacturing Regulation in the EU

In addition to an MA, various other requirements apply to the manufacture and placing on the EU market of medicinal products. The manufacture of medicinal products in the EU requires a manufacturing authorization. Moreover, import of medicinal products into the EU requires a manufacturing authorization allowing for import. The holder of a manufacturing authorization must comply with various requirements set out in the applicable EU laws, regulations and guidance, including GMP standards. Similarly, the distribution of medicinal products within the EU is subject to compliance with applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of EU member states. MA holders and/or manufacturing and import authorization, or MA holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU member states' requirements applicable to the manufacturing of medicinal products.

Post-authorization Requirements in the EU

Where an MA is granted in relation to a medicinal product in the EU, the holder of the MA is required to comply with a range of regulatory requirements applicable to the manufacture, marketing, promotion and sale of medicinal products. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the individual EU member states. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAAs must include a risk management plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

In the EU, the advertising and promotion of medicinal products are subject to both EU and EU member states' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. General requirements for advertising and promotion of medicinal products, such as direct-to-consumer advertising of prescription medicinal products are established in EU law. However, the details are governed by regulations in individual EU member states and can differ from one country to another. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics ("SmPC"), which may require approval by the competent national authorities in connection with an MA. The SmPC is the document that provides information to physicians and other healthcare professionals concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU.

The aforementioned EU rules are generally applicable in the European Economic Area (which is comprised of the 27 EU member states plus Norway, Iceland and Liechtenstein).

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Pricing, Coverage and Reimbursement in the EU

In the EU, pricing and reimbursement schemes vary widely from country to country. Some EU member states may approve a specific price for a product, or they may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

In addition, some EU member states may require the completion of additional studies that compare the cost-effectiveness of a particular medicinal product candidate to currently available therapies. This Health Technology Assessment (“HTA”), process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states.

In December 2021, Regulation No 2021/2282 on Health Technology Assessment (the “HTA Regulation”) was adopted. The Regulation is intended to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. HTA Regulation has applied from January 12, 2025, although it will enter into force iteratively and initially apply to new active substances to treat cancer and to all ATMPs, it will then be expanded to orphan medical products in January 2028, and to all centrally authorized medicinal products as of 2030. Selected high-risk medical devices will also be assessed under the HTA Regulation as of 2026. The HTA Regulation is intended to harmonize the clinical benefit assessment of HTA across the European Union.

UK Regulation

HTA Regulation has applied from January 12, 2025, although it will enter into force iteratively and initially apply to new active substances to treat cancer and to all ATMPs, it will then be expanded to orphan medicinal products in January 2028, and to all centrally authorized medicinal products as of 2030. Selected high-risk medical devices will also be assessed under the HTA Regulation as of 2026. The HTA Regulation is intended to harmonize the clinical benefit assessment of HTA across the European Union.

The UK regulatory framework in relation to clinical trials is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which is derived from the CTD, as implemented into UK national law through secondary legislation. On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials, and which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The UK government published its response to the consultation on March 21, 2023, confirming that it would bring forward changes to the legislation. The UK Government published its response to the consultation on March 21, 2023, confirming that it would bring forward changes to the legislation and such changes were laid in parliament on December 12, 2024. These resulting legislative amendments will, if implemented in their current form, bring the UK into closer alignment with the CTR. In October 2023, the MHRA announced a new Notification Scheme for clinical trials which enables a more streamlined and risk-proportionate approach to initial clinical trial applications for Phase 4 and low-risk Phase 3 clinical trial applications.

Marketing authorizations in the UK are governed by the Human Medicines Regulations (SI 2012/1916), as amended. Since January 1, 2021, an applicant for the EU’s centralized procedure marketing authorization can no longer be established in the UK. As a result, since this date, companies established in the UK cannot use the EU’s centralized procedure. To obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures. Applications are governed by the Human Medicines Regulations (SI 2012/1916) and are made electronically through the MHRA Submissions Portal. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, a 150-day assessment (subject to clock-stops) and a rolling review procedure. The rolling-review procedure permits the separate or joint submission of quality, non-clinical, and

clinical data to the MHRA which can be reviewed on a rolling basis. After an application under the rolling-review procedure has been validated, the decision should be received within 100 days (subject to clock-stops).

In addition, since January 1, 2024, the MHRA may rely on the International Recognition Procedure (“IRP”), when reviewing certain types of MAAs. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (e.g., the regulatory in Australia, Canada, Switzerland, Singapore, Japan, the United States and the EU). The MHRA will conduct a targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. The IRP allows medicinal products approved by such trusted regulatory partners that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update a MA in the UK. Applications should be decided within a maximum of 60 days if there are no major objections identified that cannot be resolved within such 60-day period and the approval from the trusted regulatory partner selected has been granted within the previous two years or if there are such major objections identified or such approval hasn’t been granted within the previous two years within 110 days. Applicants can submit initial MAAs to the IRP, but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals.

Japanese Regulation

Manufacturers and sellers of drugs, quasi-drugs, cosmetics, medical devices and regenerative medical products (“Designated Products”) in Japan are subject to the supervision of Japan’s Ministry of Health, Labour and Welfare (“MHLW”) primarily under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics of Japan (“PMDA” or “PMD Act”). Under the PMD Act, the relevant licenses must be obtained from the MHLW in order to conduct the business of manufacturing, marketing or selling Designated Products.

Applications for the approval of new products are made through the PMDA. The clinical trial data and other pertinent data must be attached to the application for approval. If the drugs, medical devices or regenerative medical products under application are of types designated by ministerial ordinance of the MHLW, the attached data mentioned above must be obtained in compliance with the standards established by the minister of the MHLW (“Minister”), such as the Good Laboratory Practice and the Good Clinical Practice. Once an application for approval is submitted, a review team is formed, which consists of specialized officials of the PMDA, including experts on chemistry/manufacturing, non-clinical, clinical, and biostatistics. Team evaluation results are passed to the PMDA’s external experts, who then report back to the PMDA. After a further team evaluation, a report is provided to the Minister; the Minister makes a final determination for approval and refers this to the Council on Drugs and Foods Sanitation, which then advises the MHLW on final approvability. Marketing and distribution approvals require a review to determine whether or not the product in the application is suitable as a drug to be manufactured and distributed with which a manufacturing and distribution business license for the type of drug concerned has been obtained, and to confirm that the product has been manufactured in a plant compliant with the GMP.

Once the MHLW has approved the application, the company can make the new drug available for physicians to prescribe. After that, the MHLW lists its National Health Insurance price within 60 days (or 90 days at the latest) from the approval, and physicians can obtain reimbursement. For some medications, the MHLW requires additional post marketing studies (Phase 4) to further evaluate safety and/or to gather information concerning the quality, efficacy, and safety of the product under specified conditions, in addition to post marketing surveillance including Early Post-marketing Phase Vigilance (“EPPV”) based on the RMP for all new medications. The MHLW also requires the drug’s sponsor to submit periodic safety update reports. Within three months from the specified re-examination period, which is designated at the time of the approval of the application for the new product, the company must submit a re-examination application to enable the drug’s quality, efficacy, and safety to be reassessed against approved labeling by the PMDA.

The PMD Act also provides for special regulations applicable to drugs, quasi-drugs, cosmetics and medical devices made of biological raw materials. These regulations impose various obligations on manufacturers and other persons in relation to manufacturing facilities, explanation to patients, labeling on products, record-keeping and reporting to the Minister.

Under the PMD Act, the Minister may take various measures to supervise manufacturing and marketing license holders of Designated Products. The Minister has the authority to order manufacturing and marketing license holders to temporarily suspend the marketing, leasing or providing of the Designated Products to prevent risks or increases in risks to the public health. Also, the Minister may revoke a license or approval granted to a manufacturing and marketing license holder or order a temporary business suspension under certain limited circumstances such as violation of laws relating to drugs.

The Hatch-Waxman Amendments

Orange Book Listing

Under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch Waxman Amendments, NDA applicants are required to identify to FDA each patent whose claims cover the applicant's drug or approved method of using the drug. Upon approval of a drug, the applicant must update its listing of patents to the NDA in timely fashion and each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book.

Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application ("ANDA"). An ANDA provides for marketing of a drug product that has the same active ingredient(s), strength, route of administration and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. An approved ANDA product is considered to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved under the ANDA pathway are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug pursuant to each state's laws on drug substitution.

The ANDA applicant is required to certify to the FDA concerning any patents identified for the reference listed drug in the Orange Book. Specifically, the applicant must certify to each patent in one of the following ways: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. For patents listed that claim an approved method of use, under certain circumstances the ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents through a Paragraph IV certification, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA-holder and patentee(s) once the ANDA has been received by the FDA for review (referred to as the "notice letter"). The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice letter. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from the date the notice letter is received, expiration of the patent, the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed, or a decision in the patent case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired. In some instances, an ANDA applicant may receive approval prior to expiration of certain non-patent exclusivity if the applicant seeks, and FDA permits, the omission of such exclusivity-protected information from the ANDA prescribing information.

Hatch-Waxman Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. For example, upon NDA approval of a new chemical entity (“NCE”), which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of non-patent data exclusivity during which FDA cannot receive (1) any ANDA seeking approval of a generic version of that drug or (2) an NDA submitted under Section 505(b)(2) of the FDCA (505(b)(2) NDA) by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication. However, an ANDA or a 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder (i.e., a Paragraph IV certification).

The FDCA also provides three years of marketing exclusivity for an NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active moiety for any other indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct, or obtain a right of reference to, all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Patent Term Extension

The Hatch Waxman Amendments permit a patent term extension as compensation for patent term lost during the FDA regulatory review process. Patent term extension, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. After NDA approval, owners of relevant drug patents may apply for the extension. The allowable patent term extension is calculated as half of the drug’s testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval) up to a maximum of five years. The time can be reduced for any time FDA determines that the applicant did not pursue approval with due diligence.

The United States Patent and Trademark Office (“USPTO”) in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. However, the USPTO may not grant an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than requested.

The total patent term after the extension may not exceed 14 years, and only one patent can be extended. The application for the extension must be submitted prior to the expiration of the patent, and for patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services (“CMS”), other divisions of the Department of Health and Human Services (“HHS”), the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

The failure to comply with regulatory requirements subjects manufacturers to possible legal or regulatory action.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. For example, the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”) and their respective implementing regulations, impose privacy, security and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities. Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal and administrative fines and penalties, and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Further, entities that knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA may be subject to criminal penalties. In addition, certain state laws govern the privacy and security of personal information, including health-related information, in certain circumstances. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, the California Consumer Privacy Act (“CCPA”) imposes certain data privacy obligations for covered companies and provides certain privacy rights to California residents. Other states have also enacted, proposed, or are considering proposing, data privacy laws. In addition, certain foreign laws govern the privacy and security of personal information, including health-related information. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Other U.S. Healthcare Laws

Pharmaceutical manufacturers are subject to numerous federal and state laws and regulations including, without limitation, state and federal anti-kickback, fraud and abuse, false claims and transparency laws, such as the following:

- federal Anti-Kickback Statute, which prohibit, among other things, persons from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a 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 statute or specific intent to violate it in order to have committed a violation;
- federal false claims laws, including the False Claim Act and the Civil Monetary Penalties Law, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, information or claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent. In addition, a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act;
- HIPAA, which prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program (including private health plans) or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the FDCA, which among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products prior to approval or for off-label use and regulates the distribution of samples;

- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- the federal Physician Payments Sunshine Act, which 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 certain exceptions) to report annually to the CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- state law equivalents of the above federal laws, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payer, including private insurers, state transparency laws, and state laws limiting interactions between pharmaceutical manufacturers and members of the healthcare industry, many of which differ from each other in significant ways and may not have the same effect, and often are not preempted by HIPAA.

U.S. Healthcare Reform

The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement, and requirements for substitution of generic products for branded prescription drugs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “ACA”) was passed which substantially changed the way healthcare is financed by both the government and private insurers and continues to significantly impact the U.S. pharmaceutical industry.

Several healthcare reform proposals culminated in the enactment of the Inflation Reduction Act (“IRA”) in August 2022, which, among other things, allows HHS to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. Only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. CMS selected the Medicare Part D products in 2023, negotiations began in 2024 and the negotiated maximum fair price for each such product has been announced. The price cap for each of these products, which cannot exceed a statutory ceiling price, will take effect in 2026. Negotiations for Medicare Part B products will begin in 2026 with the negotiated price taking effect in 2028. A drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA’s price negotiation requirements, but will lose that exclusion if it receives designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The IRA also imposes rebates on Medicare Part B and Part D drugs whose prices have increased at a rate greater than the rate of inflation, and in November 2024, CMS finalized regulations for the Medicare Part B and Part D inflation rebates. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including significant civil monetary penalties. These provisions have been and may continue to be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the biopharmaceutical industry and the pricing of prescription drug products.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and in some cases, designed to encourage importation from other countries and bulk purchasing.

Employees and Human Capital Resources

As of December 31, 2024, we had 170 employees, consisting of clinical, scientific, development, regulatory, finance, legal and operational personnel, of which 168 were full-time employees. We also retain independent contractors to support certain organizational needs. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

We recognize that our culture is central to the productivity, agility, scalability and competitiveness of our operation, and is essential to our success. We are clear and consistent in our company values and we communicate and support an employee value proposition. Our proposition is centered with unique and impactful professional development opportunities within an environment of inclusive representation and diverse thinking as a unifying force and business differentiator. Our employees are critical to our long-term success and are essential to helping us meet our goals. Among other things, we support and incentivize our employees in the following ways:

- *Talent development, compensation and retention:* Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.
- *Health and safety:* We support the health and safety of our employees by providing comprehensive insurance benefits, an employee assistance program, company-paid holidays, a personal time-off program and other additional benefits which are intended to assist employees to manage their well-being.
- *Inclusion and diversity workplace:* We are committed to an inclusive and diverse workplace because we believe that fostering an inclusive work environment with a team of employees having wide-ranging backgrounds, experiences, perspectives and skillsets enhances our corporate culture and is key to our long-term success.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. Before deciding to invest in shares of our common stock, you should carefully consider the risks described below, together with the other information contained in this Annual Report on Form 10-K, including in the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and in our audited financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. We cannot assure you that any of the events discussed below will not occur. These events could adversely impact our business, financial condition, results of operations and prospects. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risk Factors Related to the Merger

The Merger may not be completed on the terms or timeline currently contemplated, or at all. Our stockholders will be subject to a number of material risks if the Merger is not completed on the terms or timeline currently contemplated, or at all.

The consummation of the Merger is subject to numerous conditions, including (1) the approval by the ACELYRIN stockholders of the proposal to adopt the Merger Agreement (the “ACELYRIN merger proposal”), (2) the approval by our stockholders of our share issuance proposal, (3) the effectiveness of the Registration Statement on Form S-4 to be filed by us with the SEC, and (4) other customary closing conditions.

If the Merger is not completed for any reason, the price of our common stock and/or the price of ACELYRIN common stock may decline to the extent that the market price thereof reflects or previously reflected positive market assumptions that the Merger would be completed, and the benefits of the Merger would be realized. In addition, we and ACELYRIN have expended and will continue to expend significant management time and resources and have incurred and will continue to incur significant expenses due to legal, advisory, printing and financial services fees related to the Merger. These expenses must be paid regardless of whether the Merger is consummated. If the Merger is not consummated, we may be

required under certain circumstances to pay ACELYRIN a termination fee of \$10.0 million and ACELYRIN may be required under certain circumstances to pay us a termination fee of \$10.0 million. There is no assurance that the Merger will be consummated. If the Merger is not timely completed, we and ACELYRIN may have to materially alter our respective business plans, including pausing and/or terminating our current and planned clinical trials and the development of our respective product candidates. For example, we will require substantial additional financing to achieve our goals and failure to obtain additional capital when needed, at all or on acceptable terms to us, could cause us to delay, limit, reduce, or terminate its product development or future commercialization efforts. Further Alumis may suffer negative reactions from our respective employees, partners and vendors in the event the Merger is not consummated. In addition, if the Merger is not completed, we could become subject to litigation related to any failure to complete the Merger or to perform their respective obligations under the Merger Agreement.

If the Merger is not completed, we cannot assure our stockholders that these risks will not materialize and will not materially affect the business, financial results and our stock prices.

Litigation relating to the Merger, if any, could result in an injunction preventing the completion of the Merger and/or substantial costs to us.

Securities class action lawsuits and derivative lawsuits are often brought against public companies that have entered into acquisition, merger or other business combination agreements like the Merger Agreement. Even if such a lawsuit is without merit, defending against such claims can result in substantial costs and divert management time and resources. An adverse judgment could result in monetary damages, which could have a negative impact on our liquidity and financial condition. Lawsuits that may be brought against us, ACELYRIN or our respective directors and officers could also seek, among other things, injunctive relief or other equitable relief, including a request to rescind parts of the Merger Agreement already implemented and to otherwise enjoin us and ACELYRIN from consummating the Merger. One of the conditions to the closing of the Merger (the “Closing”) is that no injunction by any governmental entity having jurisdiction over us, ACELYRIN or Merger Sub has been entered and continues to be in effect and no law has been adopted, in either case, that prohibits the Closing. If a plaintiff is successful in obtaining an injunction prohibiting completion of the Merger, that injunction may delay or prevent the Merger from being completed within the expected time frame or at all, which may adversely affect our business, financial position and results of operations.

There can be no assurance that any defendants will be successful in the outcome of any potential future lawsuits. The defense or settlement of any lawsuit or claim that remains unresolved at the time the Merger is completed may adversely affect the combined company’s business, financial condition, results of operations and cash flows.

The Merger Agreement contains provisions that could discourage a potential competing acquiror of us or could result in any competing proposal being at a lower price than it might otherwise be.

The Merger Agreement contains “no-shop” provisions that, subject to limited exceptions, restrict ACELYRIN’s and our ability to solicit, encourage, facilitate or discuss competing third-party proposals to acquire all or a significant part of our company. In addition, each party generally has an opportunity to offer to modify the terms of the Merger in response to any competing acquisition proposals that may be made before the other party’s board of directors may withdraw or qualify its recommendation regarding the proposals described herein. In specified circumstances, we may be required to pay a termination fee to the other party due to the termination of the Merger Agreement.

These provisions could discourage a potential competing acquiror that might have an interest in acquiring all or a significant part of us from considering or proposing that acquisition, even if it were prepared to pay consideration with a higher value than the market value proposed to be received or realized in the Merger, or might result in a potential competing acquiror proposing to pay a lower price than it might otherwise have proposed to pay because of the added expense of the termination fee under the Merger Agreement or expenses that may become payable in certain circumstances.

If the Merger Agreement is terminated and we attempt to seek another business combination, there is no assurance that we will be able to negotiate a transaction with another party on terms comparable or better than the terms of the Merger.

The pendency of the Merger could adversely affect our business and operations of us and ACELYRIN.

In connection with the Merger, our existing or prospective partners may delay or defer decisions or reduce their level of business with either or both of the companies, any of which could negatively affect our business and financial results, regardless of whether the Merger is completed. ACELYRIN intends to delay the initiation of its previously announced Phase 3 LONGITUDE program for the evaluation of subcutaneous lonigutamab in thyroid eye disease, which may adversely impact the combined company's ability to develop lonigutamab. In addition, due to operating covenants in the Merger Agreement, we may be unable, during the pendency of the Merger, to pursue strategic transactions, undertake significant capital projects, undertake certain significant financing transactions and otherwise pursue other actions without the consent of the other party or as otherwise discussed elsewhere in these risk factors, even if such actions would prove beneficial. Our employees may experience uncertainty about their future roles with the combined company, which might adversely affect each company's ability to retain and hire key managers and other employees. Moreover, the pursuit of the Merger and the preparation for the integration of the companies may place a significant burden on the management and personnel of both companies, and the attention of the combined company's management may continue to be diverted to such matters even after consummation of the Merger. The diversion of management's attention away from operating the companies in the ordinary course could adversely affect our financial results and the advancement of their respective product candidates. Any of these effects could adversely affect our business prior to the completion of the Merger.

The Merger may be completed even if one of the parties is subject to material and adverse impacts that are excluded from the definition of material adverse effect in the Merger Agreement.

In general, neither we nor ACELYRIN is obligated to complete the Merger if there is a material adverse effect affecting the other party between February 6, 2025, the date of the Merger Agreement, and the consummation of the Merger. However, certain types of changes are excluded from the concept of a "material adverse effect." Such exclusions include, but are not limited to:

- changes or conditions generally affecting the industries in which we or ACELYRIN, as applicable, operate;
- general economic or political conditions or securities, credit, financial or other capital markets conditions, in each case in the United States or any foreign jurisdiction;
- any failure, in and of itself, by us or ACELYRIN, as applicable, to meet any internal or published projections, forecasts, estimates or predictions in respect of revenues, earnings or other financial or operating metrics for any period;
- the public announcement or pendency of the transactions contemplated hereby (including the impact on the relationships, contractual or otherwise, of such party or any of its subsidiaries with employees, labor unions, suppliers or partners);
- any change, in and of itself, in the market price or trading volume of us or ACELYRIN's, as applicable, securities or in its credit ratings;
- any change in applicable law, regulation or with accounting principles generally accepted in the United States of America;
- geopolitical conditions, the outbreak or escalation of hostilities, any acts of war, sabotage or terrorism, or any escalation;
- any hurricane, tornado, flood, earthquake or other natural disaster;
- any epidemic, pandemic or disease outbreak (including COVID-19) and any action by a governmental entity in response thereto;

- any litigation arising from allegations of a breach of fiduciary duty or other violation of applicable law relating to the Merger Agreement or the transactions contemplated thereby;
- any adverse effects, AEs or safety observations or reports of new side effects, AEs or safety observations with respect to our or ACELYRIN's, as applicable, product candidates;
- any regulatory, manufacturing or clinical effect or other action resulting from any non-clinical (including internal and external research and discovery) or clinical studies (including compassionate use studies) sponsored by us or ACELYRIN, as applicable, or any competitor of such party;
- any results of meetings with the FDA or other governmental body (including any communications from any governmental body in connection with such meetings), or any increased incidence or severity of any previously identified side effects, adverse effects, AEs or safety observations or reports of
- new side effects, AEs or safety observations with respect to our or ACELYRIN's, as applicable, product candidates or any competitor's product candidates; or
- any taking of any action required pursuant to the Merger Agreement, or not required by the Merger Agreement but taken at the written request or with the prior written consent of the other party.

If any such adverse changes occur and we and ACELYRIN consummate the Merger, the stock price of the combined company may suffer. This in turn may reduce the value of the Merger to the stockholders of us, ACELYRIN or both.

Our current stockholders will have a reduced ownership interest and voting power in the combined company after the Merger.

Immediately following the Merger, our pre-Merger stockholders are expected to hold approximately 55% of the combined company's common stock and the pre-Merger stockholders of ACELYRIN are expected to hold approximately 45% of the combined company's common stock, in each case, calculated on a fully diluted basis as of January 31, 2025.

Alumis stockholders and ACELYRIN stockholders currently have the right to vote for their respective directors and on certain other matters affecting their respective companies. If and when the Merger occurs, each Alumis stockholder will remain a stockholder of Alumis with a percentage ownership of Alumis that will be smaller than the stockholder's percentage of Alumis prior to the Merger (without considering such stockholder's current ownership of ACELYRIN shares, if any). Correspondingly, each ACELYRIN stockholder who receives shares of Alumis common stock will become an Alumis stockholder with a percentage ownership of Alumis that will be smaller than the stockholder's percentage ownership of ACELYRIN (without considering such stockholder's current ownership of our common stock, if any). Our stockholders will have less voting power in Alumis than they currently have, and former ACELYRIN stockholders will have less voting power in us than they now have in ACELYRIN. Our pre-Merger stockholders will be able to exercise less influence over the management and policies of the combined company following the consummation of the Merger than they are able to exercise over Alumis or ACELYRIN, as applicable, immediately prior to the consummation of the Merger.

Directors and executive officers of us and ACELYRIN have interests in the Merger that may be different from, or in addition to, those of other our stockholders and ACELYRIN stockholders, which could have influenced their decisions to support or approve the Merger.

In considering whether to approve the proposals at our virtual special meeting and the ACELYRIN virtual special meeting, as applicable, our and ACELYRIN stockholders should recognize that directors and executive officers of us and ACELYRIN have interests in the Merger that may differ from, or that are in addition to, their interests as our stockholders and stockholders of ACELYRIN. Alan B. Colowick, M.D., M.P.H. and Patrick Machado are members of each company's board of directors and will continue as directors of the combined company after the effective time of the Merger (the "Effective Time"), and, following the Closing, will be eligible to be compensated as non-employee directors of the combined company pursuant to our amended and restated non-employee director compensation policy that is expected to

remain in place following the Effective Time. Certain of ACELYRIN's directors have options, subject to vesting, to purchase shares of ACELYRIN common stock which, after the Effective Time, will be converted into and become options to purchase shares of the common stock of the combined company and all of ACELYRIN'S directors are entitled to certain indemnification and liability insurance coverage pursuant to the terms of the Merger Agreement. In addition, the directors and executive officers of ACELYRIN have other interests, which include, among others, severance benefits, continued indemnification and the right to accelerated vesting. For example, ACELYRIN's severance policy provides employees with cash severance payments, certain health insurance coverage and the acceleration of outstanding equity awards in the event of an involuntary termination in connection with a change of control of ACELYRIN.

Our board of directors, with Dr. Colowick and Mr. Machado recused and the ACELYRIN board of directors, with Dr. Colowick and Mr. Machado recused were aware of these interests at the time each approved the Merger Agreement. These interests may cause our and ACELYRIN's directors and executive officers to view the Merger differently than you may view it as a stockholder.

Financial projections regarding us and ACELYRIN may not prove accurate.

In connection with the Merger, we and ACELYRIN prepared and considered internal financial forecasts for us and ACELYRIN. These financial projections are based on several assumptions, including regarding future operating cash flows, expenditures and income of us and ACELYRIN, including benefits to be realized from the Merger. These financial projections were not prepared with a view to public disclosure, are subject to significant economic, competitive, industry and other uncertainties and may not be achieved in full, within projected timeframes or at all. The failure of Alumis and ACELYRIN to achieve projected results could have a material adverse effect on the price of each company's common stock prior to consummation the Merger and the combined company's financial position after the consummation of the Merger.

The combined company may fail to realize the anticipated benefits of the Merger.

The success of the Merger will depend on, among other things, the combined company's ability to combine our and ACELYRIN's businesses in a manner that realizes anticipated synergies and meets or exceeds the forecasted cash balances and expense levels anticipated by each company. On a combined basis, the combined company expects to benefit from each of our and ACELYRIN's product pipelines and the potential market opportunity for each company's product candidates, if approved. If the combined company is not able to successfully achieve these objectives, then the anticipated benefits of the Merger may not be realized fully or at all or may take longer to realize than expected.

The failure to successfully integrate the businesses and operations of us and ACELYRIN in the expected time frame may adversely affect the combined company's future results.

We and ACELYRIN have operated and, until the completion of the Merger, will continue to operate independently. There can be no assurances that their businesses can be integrated successfully. It is possible that the integration process could result in the loss of our key employees or key ACELYRIN employees, the disruption of either company's or both companies' ongoing businesses, inconsistencies in standards, controls, procedures and policies, unexpected integration issues, higher than expected integration costs and an overall post-completion integration process that takes longer than originally anticipated.

Specifically, the following issues, among others, must be addressed in integrating the operations of us and ACELYRIN in order to realize the anticipated benefits of the Merger so the combined company performs as expected:

- combining the companies' operations and corporate functions;
- reducing additional and unforeseen expenses such that integration costs more than anticipated;
- avoiding delays in connection with the Merger or the integration process;

- integrating personnel from the two companies and minimizing the loss of key employees;
- identifying and eliminating redundant and underperforming functions and assets;
- harmonizing the companies' operating practices, employee development and compensation programs, internal controls and other policies, procedures and processes;
- maintaining existing agreements with distributors, providers and vendors and avoiding delays in entering into new agreements with distributors, providers and vendors;
- addressing possible differences in business backgrounds, corporate cultures and management philosophies; and
- consolidating the companies' administrative and information technology infrastructure and financial systems.

In addition, at times the attention of certain members of either company's or both companies' management and resources may be focused on completion of the Merger and the integration of the businesses of the two companies and diverted from day-to-day business operations or other opportunities that may have been beneficial to such company, which may disrupt each company's ongoing business and the business of the combined company.

Failure to attract, motivate and retain executives and other key employees could diminish the anticipated benefits of the Merger.

The success of the Merger will depend in part on the retention of personnel critical to the business and operations of the combined company due to, for example, their technical skills or management expertise.

Competition for qualified personnel can be intense. Current and prospective employees of us and ACELYRIN may experience uncertainty about their future role with us, ACELYRIN or the combined company until strategies with regard to these employees are announced or executed, which may impair our and ACELYRIN's ability to attract, retain and motivate key management, sales, marketing, technical and field personnel, prior to and following the Merger. Employee retention may be particularly challenging during the pendency of the Merger, as employees of our and ACELYRIN may experience uncertainty about their future roles with us. If we and ACELYRIN are unable to retain personnel, including our and ACELYRIN's key management, who are critical to the successful integration and future operations of the companies, we and ACELYRIN could face disruptions in their operations, loss of key information, expertise or know-how, and unanticipated additional recruitment and training costs. In addition, the loss of key personnel could diminish the anticipated benefits of the Merger.

If key employees of us or ACELYRIN depart, the integration of the companies may be more difficult and Alumis' business following the Merger may be harmed. Furthermore, we may have to incur significant costs in identifying, hiring and retaining replacements for departing employees and may lose significant expertise and talent relating to the business of each of us and ACELYRIN, and the combined company's ability to realize the anticipated benefits of the Merger may be adversely affected. In addition, there could be disruptions to or distractions for the workforce and management associated with integrating employees into our business. No assurance can be given that, following completion of the Merger, Alumis will be able to attract or retain key employees of us and ACELYRIN to the same extent that those companies have been able to attract or retain their own employees in the past.

Risks Related to Our Financial Position and Need for Capital

We are a clinical stage biopharmaceutical company with a limited operating history and no products approved for commercial sale, and have incurred substantial losses since our inception and anticipate incurring substantial and increasing losses for the foreseeable future.

We are a clinical stage biopharmaceutical company with a limited operating history on which to base your investment decision. We have no product candidates approved for commercial sale and have not generated any revenue.

Biopharmaceutical product development is a highly speculative undertaking. It entails substantial upfront capital expenditures and significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval or become commercially viable.

Our most advanced candidate is ESK-001, an oral, small molecule allosteric inhibitor of TYK2. We are currently conducting two parallel Phase 3 clinical trials of ESK-001 in PsO and a Phase 2b clinical trial of ESK-001 in SLE. In addition, we are advancing A-005, an investigational CNS penetrant allosteric inhibitor of TYK2 that has a potential application in MS and other neuroinflammatory and neurodegenerative diseases, currently in Phase 1 clinical development. Our ability to achieve profitability in the future is dependent upon obtaining regulatory approval for and successfully commercializing our most advanced candidate, ESK-001, either alone or with third parties. However, our operations may not be profitable even if ESK-001 is successfully developed, approved and thereafter commercialized.

We have and will continue to incur significant development and other expenses related to our research and clinical development programs and ongoing operations. For the years ended December 31, 2024 and 2023, our net losses were \$294.2 million and \$155.0 million, respectively. As of December 31, 2024, we had an accumulated deficit of \$658.6 million. Substantially all of our losses have resulted from expenses incurred in connection with the acquisition and development of our pipeline and from general and administrative costs associated with our operations. We expect to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our development of our product candidates. Likewise, we expect to incur substantial costs and expenses in connection with completing the Merger and integrating ACELYRIN's business. While we expect that a certain level of transaction and integration costs and expenses would be incurred, there are a number of factors beyond our control that could affect the total amount or the timing of its integration costs and expenses, including any ACELYRIN liabilities that arise, or become known, following the Closing. Many of the costs and expenses that will be incurred, by their nature, are difficult to estimate accurately at the present time. Due to these factors, the transaction and integration costs and expenses could be greater or could be incurred over a longer period of time than we currently expect.

We anticipate that our expenses will increase substantially if, and as, we:

- conduct preclinical studies and clinical trials for ESK-001, A-005, and other programs;
- identify additional product candidates and acquire rights from third parties to those product candidates through licenses or other acquisitions, and conduct development activities, including preclinical studies and clinical trials;
- procure the manufacturing of preclinical, clinical and commercial supply of our current and future product candidates;
- seek regulatory approvals for our current or any future product candidates;
- commercialize our current or any future product candidates, if approved;
- take steps toward our goal of being an integrated biopharma company capable of supporting commercial activities, including establishing sales, marketing and distribution infrastructure;
- attract, hire and retain qualified clinical, scientific, operations and management personnel;
- add and maintain operational, financial and information management systems;
- protect, maintain, enforce and defend our rights in our intellectual property portfolio;
- defend against third-party interference, infringement and other intellectual property claims, if any;

- address any competing therapies and market developments;
- experience any delays in our preclinical studies or clinical trials and seeking regulatory approval for our product candidates due to public health concerns, macroeconomic conditions or geopolitical conflicts; and
- incur costs associated with operating as a public company.

Even if we succeed in commercializing one or more product candidates, we expect to incur substantial development costs and other expenditures to develop and market additional product candidates. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue or raise additional capital. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity (deficit) and our working capital.

We could also encounter delays if a clinical trial is suspended, put on clinical hold or terminated by us, the IRBs or ethics committees of the institutions in which such trials are being conducted, the FDA, or other comparable foreign regulatory authorities, or if a clinical trial is recommended for suspension or termination by the Data Safety Monitoring Board for such trial. A suspension, clinical hold or termination may be imposed due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, failure by our contract research organizations ("CROs") or clinical trial sites to perform in accordance with GCPs, or applicable regulatory guidelines in other countries, inspection of the clinical trial operations or trial site by the FDA or other comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. For example, we discontinued our proof-of-concept Phase 2a clinical trial of ESK-001 in patients with non-infectious uveitis in June 2024 based on the efficacy results of a data analysis prepared for a scheduled monitoring committee meeting, which efficacy results did not meet our clinical threshold for success despite safety results consistent with ESK-001's safety profile in psoriasis patients. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other comparable foreign regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

We may also, in the future, conduct preclinical and clinical research in collaboration with other academic, pharmaceutical and biotechnology entities in which we combine our research or development efforts with those of our collaborators. Such collaborations may be subject to additional delays because of the management of the trials, contract negotiations, the need to obtain agreement from multiple parties and may increase our future costs and expenses.

Our product development costs will increase if we experience delays in clinical testing or regulatory approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates. Any delays or increase in costs in our clinical development programs may harm our business, financial condition, results of operations and prospects.

Enrollment and retention of participants in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, including difficulties in identifying patients, the availability of competitive products, and significant competition for recruiting participants in clinical trials.

Participant enrollment, a significant factor in the timing of clinical trials, is affected by many conditions, including the size and nature of the patient population, the number and location of clinical sites we enroll, the proximity of participants to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the inability to obtain and maintain participant consents, the risk that enrolled participants will drop out before completion, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation

to other available therapies, including any new drugs or biologics that may be approved for the indications being investigated by us. Risks related to patient enrollment are heightened in longer clinical trials, including the 48-week trial period contemplated by our ongoing Phase 2b clinical trial of ESK-001 in SLE. In particular, this trial has been and may continue to be challenging to enroll due to the fact that patients must be experiencing active disease at the time of screening to be eligible for enrollment. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same areas as our product candidates, and this competition will reduce the number and types of participants available to us, because some participants who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors, or to use currently marketed therapies. Additionally, participants, including participants in any control groups, may withdraw from the clinical trial if they are not experiencing improvement in their underlying disease or condition or if they experience other difficulties or issues. Additionally, we could encounter delays if treating clinicians encounter unresolved ethical issues associated with enrolling participants in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles.

We have in the past experienced and expect to continue to experience participant withdrawals or discontinuations from our trials. For example, as long-term treatment with ESK-001 continues to be evaluated in our STRIDE OLE, ONWARD3 LTE study and LUMUS Part B OLE, we expect to see discontinuation rates rise over time. Withdrawal of participants from our clinical trials may compromise the quality of our data. Even if we are able to enroll a sufficient number of participants in our clinical trials, delays in enrollment or small population size may result in increased costs or may affect the timing or outcome of our clinical trials. Any of these conditions may negatively impact our ability to complete such trials or include results from such trials in regulatory submissions, which could adversely affect our ability to advance the development of our product candidates.

We will require substantial additional financing to achieve our goals and failure to obtain additional capital when needed, or on acceptable terms to us, could cause us to delay, limit, reduce, or terminate our product development or future commercialization efforts.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, including potential collaborations, licenses and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of our common stock. Any future debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan. We could also be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

As a result of our recurring losses from operations and recurring negative cash flows from operations, our management concluded that there is a substantial doubt about our ability to maintain liquidity sufficient to operate our business effectively, which raises substantial doubt about our ability to continue as a going concern. See the risk factor below titled, “As a result of our history of losses and negative cash flows from operations, our consolidated financial statements contain a statement regarding a substantial doubt about our ability to continue as a going concern.” Based on our current operating plan, we will need to raise additional financing to continue our products’ development for the foreseeable future, and until we become profitable. Any additional fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize product candidates. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to obtain funding when and as needed on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Risks Related to Product Candidate Development and Commercialization

Preclinical and clinical development involves a lengthy and expensive process, with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates.

Our product candidates are either in clinical or preclinical development, and their risk of failure is high. It is impossible to predict when or if our product candidates will receive regulatory approval. To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and lengthy, complex and expensive clinical trials that our product candidates are safe and effective in humans for their intended uses. Before obtaining approval from regulatory authorities for the commercialization of any of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate in humans. Before we can initiate clinical trials for any product candidates, we must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND application or similar regulatory submission. The FDA or comparable foreign regulatory authorities may require us to conduct additional preclinical studies for any product candidate before allowing us to initiate clinical trials under any IND or similar regulatory submission, which may lead to delays and increase the costs of our preclinical development programs.

Once initiated, clinical testing can take many years to complete, and its outcome is inherently uncertain. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials and results in one indication may not be predictive of results to be expected for the same product candidate in another indication. For example, notwithstanding extensive preclinical testing demonstrating that A-005 can penetrate the CNS, our clinical trials of A-005 may show that it cannot penetrate the human CNS as fully as was observed in preclinical testing. Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unfavorable safety profiles, notwithstanding promising results in earlier trials, and we have experienced and may experience setbacks in our programs in the future. For example, we discontinued our proof-of-concept Phase 2a clinical trial of ESK-001 in patients with non-infectious uveitis in June 2024 based on the efficacy results of a data analysis prepared for a scheduled monitoring committee meeting, which efficacy results did not meet our clinical threshold for success despite safety results consistent with ESK-001's safety profile in psoriasis patients. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain regulatory approval of such product candidates.

Commencing any future clinical trials is subject to finalizing the trial design and submitting an application to the FDA or a comparable foreign regulatory authority. Even after we make our submission, the FDA or comparable foreign regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or disagree with our study design, which may require us to complete additional trials or amend our protocols or impose stricter conditions on the commencement of clinical trials. There is typically a high rate of failure of product candidates proceeding through clinical trials, and failure can occur at any time during the clinical trial process. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our current or future clinical trials will ultimately be successful or support the approval of our current or any future product candidates.

We expect to continue to rely on our CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, including the participant enrollment process, and we have limited influence over their performance. We or any future collaborators may experience delays in initiating or completing clinical trials due to unforeseen events or otherwise, that could delay or prevent our ability to receive regulatory approval or commercialize our current and any future product candidates, including:

- we may be unable to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;

- regulators, such as the FDA or comparable foreign regulatory authorities, may disagree with the design or implementation of our clinical trials;
- regulators, such as the FDA or comparable foreign regulatory authorities, IRBs, or ethics committees may impose additional requirements before permitting us to initiate a clinical trial, may not allow us or our investigators to commence or conduct a clinical trial at a prospective trial site, may not allow us to amend trial protocols, or regulators may require that we modify or amend our clinical trial protocols;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with trial sites and CROs, the terms of which can be subject to extensive negotiation and may vary significantly;
- we may be unable to identify, recruit, or train suitable clinical investigators;
- clinical trial sites may deviate from trial protocol or drop out of a trial;
- we may be unable to complete our clinical trials due to trial participant withdrawals and discontinuations due to AEs;
- the number of participants required for clinical trials may be larger than we anticipate, enrollment in clinical trials may be slower than we anticipate or participants may drop out or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- the cost of clinical trials may be greater than we anticipate, or we may have insufficient funds to initiate or complete a clinical trial or to pay the substantial user fees required by the FDA upon the submission of a New Drug Application or comparable marketing authorization application in another jurisdiction;
- the quality or quantity of data relating to our product candidates or other materials necessary to conduct our clinical trials may be inadequate to initiate or complete a given clinical trial;
- reports from clinical testing of other therapies may raise safety, tolerability or efficacy concerns about our product candidates;
- clinical trials of our product candidates may fail to show appropriate safety, tolerability or efficacy, may produce negative or inconclusive results, or may otherwise fail to improve on the existing standard of care, and we may decide, or regulators may require us, to conduct additional clinical trials or we may decide to abandon product development programs;
- our CROs or clinical trial sites may fail to perform in accordance with GCP requirements or other applicable regulations, rules or guidelines;
- we may be unable to manufacture our product candidates from our contract manufacturing organizations (“CMOs”) in accordance with current Good Manufacturing Practice (“cGMP”) regulations or other applicable requirements in sufficient quantities for use in our clinical trials;
- SAEs may occur in our clinical trials or in trials of the same class of agents conducted by other companies that could be considered similar to our product candidates;
- we may select clinical endpoints that require prolonged periods of clinical observation or extended analysis of the resulting data;
- we may be required to transfer our manufacturing processes to larger-scale facilities operated by a different CMO, or may experience delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and

- third parties may be unwilling or unable to satisfy their contractual obligations to us in a timely manner.

In addition, we have historically leveraged our extensive analyses of immune-relevant genome-wide association study results from both the public domain and the UK Biobank biomedical resource to identify the right therapeutic target on which to focus our preclinical and clinical development efforts. If our access to GWAS results from the public domain or the UK Biobank biomedical resource were to be restricted, including as a result of any potential future legislative policies or regulations that may seek to restrict the sharing of genetic data, our ability to efficiently identify additional therapeutic targets may be limited.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. In the EU, the EU Clinical Trials Regulation ("CTR") became applicable on January 31, 2022, repealing and replacing the Clinical Trials Directive ("CTD"). The CTR permits trial sponsors to make a single submission to both the competent authority and an ethics committee in each EU member state, leading to a single decision for each EU member state. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment of some elements of the application by all EU member states in which the trial is to be conducted, and a separate assessment by each EU member state with respect to specific requirements related to its own territory, including ethics rules. Each EU member state's decision is communicated to the sponsor through a centralized EU portal, the Clinical Trial Information System. The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR.

It is currently unclear to what extent the UK, will seek to align its regulations with the EU in the future. The UK regulatory framework in relation to clinical trials is derived from existing legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The UK government published its response to the consultation outcome on March 21, 2023, confirming that it would bring forward changes to the legislation and such changes were laid in parliament on December 12, 2024. These resulting legislative amendments will, if implemented in their current form, bring the UK into closer alignment with the CTR. Failure of the UK to closely align its regulations with the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization for our product candidates on the basis of clinical trials conducted in the UK.

Our clinical trials may reveal SAEs and AEs and may result in a safety or tolerability profile that could delay or prevent regulatory approval or market acceptance of ESK-001, A-005 or any future product candidates.

Undesirable or clinically unmanageable side effects observed in our clinical trials for our product candidates could occur and cause us or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive labeling or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities.

We have observed SAEs and AEs in our trials of ESK-001, and as more patients become exposed to ESK-001 over longer periods of time, we expect to see additional SAEs and AEs emerge. Further, long term treatment with ESK-001 continues to be evaluated in an OLE trial, and additional AEs and SAEs will continue to accumulate. Certain conditions occur more frequently in patients with psoriasis compared to the general population. Examples include obesity, cardiovascular disease, psoriatic arthritis, and depression. Immune modulating treatments including ESK-001 may result in increasing susceptibility to various infections, including serious or life-threatening infections, and there is a theoretical risk with immune-modulating agents that dampening immune responses could increase the risk of malignancies.

Other TYK2 inhibitors, such as deucravacitinib (marketed as Sotyktu), which is approved for the treatment of adults with PsO, have shown AEs such as hypersensitivity reactions, infections, tuberculosis, malignancy and rhabdomyolysis. The label for deucravacitinib includes a warning concerning the potential for JAK-related AEs, such as cardiovascular and thrombotic events. We have observed, and expect that additional AEs and SAEs consistent with known side effects of TYK2 inhibition may emerge, in our ongoing and future clinical trials of ESK-001.

The most common AEs observed in our Phase 2 STRIDE and OLE PsO trials that were considered related to ESK-001 treatment by the principal investigator include headaches, upper respiratory tract infections, nasopharyngitis, rash and nausea. As of December 31, 2024, there were four SAEs from the STRIDE OLE trial that were considered related to

ESK-001 treatment by the investigator: one serious infection case (peritonsillar abscess), two malignancy cases (non-small cell lung cancer, renal cell carcinoma), and one arthritis case. We continue to evaluate the safety profile of ESK-001 in our ongoing Phase 2 OLE and Phase 3 trials.

If AEs, SAEs or other side effects are observed in any of our ongoing or future clinical trials that are atypical of, or more severe than, the known side effects of the respective class of agents that each of our product candidates are a part of, we may have difficulty recruiting participants to our clinical trials, participants may drop out of our trials, or we may be required to abandon those trials or our development efforts of one or more product candidates altogether. If such effects are more severe or less reversible than we expect, or not reversible at all, we may decide or be required to perform additional studies or to halt or delay further clinical development of ESK-001, A-005 or any future product candidates, which could result in the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities.

If ESK-001 fails to demonstrate an acceptable benefit/risk profile, versus current approved therapies or others in clinical development, then our opportunity to disrupt the current standard of care may be limited. AEs and SAEs that emerge during clinical investigation of or treatment with ESK-001, A-005, or any future product candidates have in the past been and may in the future be deemed to be related to our product candidates. This may require longer and more extensive clinical development, or regulatory authorities may increase the amount of data and information required to approve, market, or maintain ESK-001, A-005 or any future product candidates and could result in warnings and precautions in our product labeling or a restrictive REMS or comparable foreign strategies. This may also result in an inability to obtain approval of ESK-001, A-005 or any future product candidates. We, the FDA or other comparable foreign regulatory authorities, or an IRB or ethics committee, may suspend clinical trials of a product candidate at any time for various reasons, including a belief that participants in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential product candidates developed in the biotechnology industry that initially showed promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining regulatory approval, undesirable side effects, like those mentioned above, may limit market acceptance of the approved product due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition, results of operations and prospects.

Additionally, if any of our product candidates receives regulatory approval, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result. For example, the FDA could require us to adopt a REMS, to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or comparable foreign strategies or engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Other potentially significant negative consequences associated with AEs include:

- we may be required to suspend marketing of a product, or we may decide to remove such product from the marketplace;
- regulatory authorities may withdraw, suspend or change their approvals of a product;
- regulatory authorities may require additional warnings on the label or limit access of a product to selective specialized centers with additional safety reporting and with requirements that patients be geographically close to these centers for all or part of their treatment; and
- we may be required to create a medication guide outlining the risks of a product for patients, or to conduct post-marketing studies.

Any of these events could diminish the usage or otherwise limit the commercial success of our product candidates and prevent us from achieving or maintaining market acceptance of our product candidates, if approved by the FDA or comparable foreign regulatory authorities.

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

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which are based on preliminary analyses of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular preclinical study or clinical trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose data from interim analyses from our clinical trials. Interim analyses from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as participants enrollment continues and more participant data become available or as participants from our clinical trials continue other treatments for their disease. Adverse differences between interim data, topline data, or preliminary data and final data could significantly harm our business prospects.

Further, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and could adversely affect the success of our business. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects. Further, disclosure of interim, top-line or preliminary data by us or by our competitors could result in volatility in the price of our common stock.

We have conducted, are currently conducting, and may in the future conduct, clinical trials for current or future product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We have conducted, are currently conducting, and may in the future conduct, clinical trials outside the United States, including (without limitation) in the EU, the UK, Japan, Latin America and APAC countries. We expect to continue to conduct trials internationally in the future. The acceptance of data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authorities 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 regulatory 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 and (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 regulatory 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 requirements for clinical data gathered outside of their respective jurisdictions. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept

data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop being delayed or not receiving approval for commercialization in the applicable jurisdiction.

Even if we receive regulatory approval for our current or future product candidates in the United States, we may never receive regulatory approval to market outside of the United States.

We plan to seek regulatory approval for our current and future product candidates outside of the United States and are currently conducting certain clinical trials internationally, including in the EU and Japan. In order to market any product outside of the United States, however, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other applicable countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ substantially from that required to obtain FDA approval. The regulatory approval processes in other countries generally implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others and would impair our ability to market our current or future product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could adversely affect our business, financial condition, results of operations and prospects.

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

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs, such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve coverage and acceptable levels of reimbursement for our products by third-party payors will have an effect on our ability to successfully commercialize those products. Even if we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the EU, Japan or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for biopharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when equivalent generic drugs, biosimilars or less expensive therapies are available. It is possible that a third-party payor may consider our product candidates, if approved, as substitutable and only be willing to cover the cost of the alternative product. Even if we show improved efficacy, safety or improved convenience of administration with ESK-001, A-005 or any of our future product candidates, if approved, pricing of competitive products may limit the amount we will be able to charge for our product candidates, if approved. Third-party payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. In some cases, when new competitor generic and biosimilar products enter the market, there are mandatory price reductions for the innovator compound. In other cases, payors employ “therapeutic category” price referencing and seek to lower the reimbursement levels for all treatments in the respective therapeutic category. Additionally, new competitor brand drugs can trigger therapeutic category reviews in the interest of modifying coverage and/or reimbursement levels. The potential of third-party payors to introduce more challenging price negotiation methodologies could have a negative impact on our ability to successfully commercialize our product candidates, if approved.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered. Some third-party payors may require pre-approval of coverage for new or innovative devices or therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products, if approved.

Obtaining and maintaining reimbursement status is time consuming, costly and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, biopharmaceutical products and services are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Some countries provide that products may be marketed only after an agreement on reimbursement price has been reached. Such pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Other countries allow companies to establish their own prices for medical products but monitor and control company profits or control prescription volumes and issue guidance to physicians to limit prescriptions. In addition, some EU member states may require the completion of additional studies that compare the cost-effectiveness of a particular medicinal product candidate to currently available therapies. This Health Technology Assessment, process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states.

Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates, if approved. In December 2021, the HTA Regulation was adopted. The HTA Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at EU level for joint clinical assessments in these areas. The HTA Regulation entered into application on January 12, 2025 and has a phased implementation. Individual EU member states continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale 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. There can be no assurance that any country that has reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

We face competition from entities that have made substantial investments into the rapid development of competitor treatments for immunological indications, including large and specialty pharmaceutical and biotechnology companies, many of which already have approved therapies in our current indications.

The development and commercialization of therapies is highly competitive. Our product candidates, if approved, will face significant competition, including from well-established, currently marketed therapies, and our failure to demonstrate a meaningful improvement to the existing standard of care may prevent us from achieving significant market penetration. Many of our competitors have significantly greater resources and experience than we do, and we may not be able to successfully compete. We face substantial competition from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. Our competitors compete with us on the level of the technologies employed, or on the level of development of their products as compared to our product candidates. In addition, many small biotechnology companies have formed collaborations with large, established companies to (i) obtain support for their research, development and commercialization of products or (ii) combine several treatment approaches to develop longer lasting or more efficacious treatments that may potentially directly compete with our current or any future product candidates. We anticipate that we will continue to face increasing competition as new therapies and combinations thereof, and related data, emerge.

Our current product candidates initially under development for treatment of patients with immune-mediated diseases, if approved, would face competition from existing approved immunological treatments, many of which have achieved commercial success. For example, we are currently developing ESK-001 for the treatment of PsO and SLE. Other emerging and established life sciences companies have been focused on similar therapeutics and indications. If approved, ESK-001 would compete with several currently approved or late-stage oral clinical therapeutics in each such indication as well as other drugs used to treat such patients.

We are also developing A-005, which has potential applications in MS and other neuroinflammatory and neurodegenerative diseases. There are several therapies available for the treatment of relapsing forms of MS, including interferon beta regulators, monoclonal antibodies, synthetic immunomodulatory drugs and S1P receptor modulators.

To compete successfully, we need to disrupt these currently marketed drugs, meaning that we will have to demonstrate that the relative cost, method of administration, safety, tolerability and efficacy of our product candidates provide a better alternative to existing and new therapies. Our commercial opportunity and likelihood of success will be reduced or eliminated if our product candidates are not ultimately demonstrated to be safer, more effective, more conveniently administered, or less expensive than the current standard of care. Furthermore, even if our product candidates are able to achieve these attributes, acceptance of our products may be inhibited by the reluctance of physicians to switch from existing therapies to our products, or if physicians choose to reserve our products for use in limited circumstances.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we have. If we obtain regulatory approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our current or any future product candidates, the ease with which our current or any future product candidates can be administered and the extent to which participants accept relatively new routes of administration, the timing and scope of regulatory approvals for these product candidates, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our current or any future product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified management and other personnel in establishing clinical trial sites and enrolling patients in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Risks Related to Our Business and Operations

Our business is highly dependent on the success of our most advanced product candidate, ESK-001, and we cannot guarantee that ESK-001 will successfully complete development, receive regulatory approval or be successfully commercialized. If we are unable to develop, receive regulatory approval for, and ultimately successfully commercialize our product candidates, or if we experience significant delays in doing so, our business will be materially harmed.

We currently have no products approved for commercial sale or for which regulatory approval to market has been sought. We have invested a significant portion of our efforts and financial resources in the development of our most advanced product candidate, ESK-001, which is still in clinical development, and expect that we will continue to invest heavily in ESK-001, as well as our second product candidate, A-005, and any future product candidates we may develop. Additionally, in connection with the anticipated consummation of the Merger, we will be evaluating the development program for lonigutamab, ACELYRIN's lead product candidate, and its potential differentiation in a capital efficient manner. Our business and our ability to generate revenue, which we do not expect will occur for many years, if ever, are substantially dependent on our ability to develop, obtain regulatory approval for, and then successfully commercialize our product candidates, which may never occur.

Our product candidates will require substantial additional preclinical and clinical development time, regulatory approval, commercial manufacturing arrangements, establishment of a commercial organization, significant marketing efforts, and further investment before we can generate any revenue from product sales. We currently generate no revenue, and we may never be able to develop or commercialize any products. We cannot assure you that we will meet our timelines for our current or future clinical trials, which may be delayed or not completed for a number of reasons, including the negative impacts of geopolitical instability, public health crises, labor shortages, inflation or other macroeconomic factors impacting our third-party CROs, CMOs, clinical trial sites, investigators or us. Our product candidates are susceptible to the risks of failure inherent at any stage of product development, including the appearance of unexpected AEs or failure to achieve primary endpoints in clinical trials. For example, we discontinued our proof-of-concept Phase 2a clinical trial of ESK-001 in patients with non-infectious uveitis in June 2024 based on the efficacy results of a data analysis prepared for a scheduled monitoring committee meeting, which efficacy results did not meet our clinical threshold for success despite safety results consistent with ESK-001's safety profile in psoriasis patients. Additionally, we may in the future advance ESK-001, A-005 or future product candidates into clinical trials and terminate such trials prior to their completion.

Even if our product candidates are successful in clinical trials, we are not permitted to market or promote our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive sufficient regulatory approval that will allow us to successfully commercialize any product candidates. If we do not receive FDA or comparable foreign regulatory approval with the necessary conditions to allow commercialization, we will not be able to generate revenue from those product candidates in the United States or elsewhere in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing our product candidates could adversely affect our business, financial condition, results of operations and prospects.

We have not previously submitted an NDA or similar marketing application to the FDA or comparable foreign regulatory authorities for any product candidate, and we cannot be certain that our current or any future product candidates will be successful in clinical trials or receive regulatory approval. The FDA may also consider its approvals of competing products, which may alter the treatment landscape concurrently with their review of any NDA we may submit, and which may lead to changes in the FDA's review requirements that have been previously communicated to us and our interpretation thereof, including changes to requirements for clinical data or clinical study design. Such changes could delay approval or necessitate withdrawal of any such NDA submission. Similar risks may exist in foreign jurisdictions.

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

- price our products competitively such that third-party and government reimbursement permits broad product adoption;

- demonstrate the superiority of our products compared to the standard of care, as well as to other therapies in development;
- create market demand for our product candidates through our own marketing and sales activities, and any other arrangements to promote these product candidates that we may otherwise establish;
- receive regulatory approval for the targeted patient populations and claims that are necessary or desirable for successful marketing;
- effectively commercialize any of our products that receive regulatory approval;
- manufacture product candidates through CMOs in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter;
- establish and maintain agreements with wholesalers, distributors, pharmacies, and group purchasing organizations on commercially reasonable terms;
- obtain, maintain, protect and enforce patent and other intellectual property protection and regulatory exclusivity for our products;
- achieve market acceptance of our products by patients, the medical community, and third-party payors;
- maintain a distribution and logistics network capable of product storage within our specifications and regulatory guidelines, and further capable of timely product delivery to commercial clinical sites; and
- assure that our product will be used as directed and that additional unexpected safety risks will not arise.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable foreign regulatory authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval of an NDA from the FDA. Similar approvals are required in order to market product candidates in foreign countries. The process of obtaining such regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA and comparable foreign regulatory authorities have substantial discretion in the approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we must demonstrate based on adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Clinical testing is expensive, time consuming and subject to uncertainty. We cannot guarantee that any current or future clinical trials will be conducted as planned or completed on schedule, if at all, or that our product candidates will receive regulatory approval. Our Phase 3 pivotal trials of ESK-001 in PsO, even if successfully completed, may not be sufficient for approval of ESK-001 in that disease. Although we have discussed and intend to further discuss our Phase 3 clinical trial design and overall development plan with the FDA to align on its sufficiency to support an NDA submission, the feedback is typically non-binding and dependent on the strength of the ultimate clinical data and the FDA's perspective on the benefit-risk profile of the treatment in the intended population. For example, the Committee for Medicinal Products for Human Use in the EU provided comments on the length of our two pivotal 24-week Phase 3 trials, and we plan to address their feedback with our

comparator trials. These modifications could delay our development timelines for EU regulatory approval and require substantially more resources. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. In addition to our Phase 3 program in PsO, which we announced in July 2024 had commenced patient dosing, we have initiated the first of potentially two pivotal Phase 2 trials of ESK-001 in SLE. Even as these trials progress, issues may arise that could require us to suspend or terminate such clinical trials or could cause the results of one cohort to differ from a prior cohort. For example, we may experience slower than anticipated enrollment in our clinical trials, which may consequently delay our development timelines or permit competitors to obtain approvals that may alter our strategy. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or comparable foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the clinical trials are not satisfactory to the FDA or comparable foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional clinical trials in support of potential approval of our product candidates.

In addition, if the FDA or comparable foreign regulatory authorities grant approval for our product candidates, then, as a condition for approval, the FDA or comparable foreign regulatory authorities may require us to perform costly post-marketing testing, including Phase 4 clinical trials or surveillance to monitor the effects of the marketed product.

Our clinical trial results may also not support approval. In addition, our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval, including due to the heterogeneity of patient populations, or apparent improvement in trial participants receiving placebo;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- The data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of an NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- such authorities may disagree with us regarding the formulation, labeling and/or the product specifications of our product candidates;
- approval may be granted only for indications that are significantly more limited than those sought by us, and/or may include significant restrictions on distribution and use;
- the FDA or comparable foreign regulatory authorities will review CMOs' manufacturing process and inspect our CMOs' commercial manufacturing facilities and may not approve our CMOs' manufacturing process or facilities with respect to our product candidates; 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 for approval.

Even if we eventually complete clinical trials and receive approval of an NDA or comparable foreign marketing application for our product candidates, the FDA or comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials and/or the implementation of a REMS or comparable foreign strategies, which may be required because the FDA or comparable foreign regulatory authority believes it is necessary to ensure safe use of the product after approval. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, FDA and foreign regulatory authorities may change their policies and new regulations may be enacted. For instance, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation and on April 10, 2024, the parliament adopted its related position. The proposed revisions remain to be agreed and adopted by the European Council. Moreover, on December 1, 2024, a new European Commission took office. The proposal could, therefore, still be subject to revisions. If adopted in the form proposed, the European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a number of changes to the regulatory framework governing medicinal products, including a decrease in data and market exclusivity opportunities for our product candidates in the EU and make them open to generic or biosimilar competition earlier than is currently the case with a related reduction in reimbursement status.

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

The ability of the FDA and comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or comparable foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or comparable foreign regulatory authorities' ability to perform routine functions. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies or comparable foreign authorities may also slow the time necessary for new drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies or regulatory authorities, 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 authorities, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the global COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations, any resurgence of the virus or emergence of new variants may lead to inspectional or administrative delays. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other comparable foreign regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other comparable foreign regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

There is substantial uncertainty regarding the new administration's initiatives and how these might impact the FDA, its implementation of laws, regulations, policies and guidance and its personnel. Similar initiatives may also be directed toward other government agencies. These initiatives could prevent, limit or delay development and regulatory approval of our product candidates, which would adversely affect our business.

FDA-regulated industries, such as ours, face substantial uncertainty with regard to the regulatory environment we will face as we proceed with research and development, and possibly in the future commercialization, efforts following the inauguration of President Trump in January 2025. Some of these efforts have manifested to date in the form of personnel measures that could impact the FDA's ability to hire and retain key personnel, which could result in delays or limitations

on our ability to obtain guidance from the FDA on our product candidates in development and obtain the requisite regulatory approvals in the future. Moreover, the new administration has proposed action to freeze or reduce the budget of the National Institute of Health (“NIH”) as related to its funding for medical research, which could decrease the ability of facilities that rely on NIH funding to enroll and conduct clinical trials or increase the costs to us of conducting clinical trials. There remains general uncertainty regarding future activities. The new administration could issue or promulgate executive orders, regulations, policies or guidance that adversely affect us or create a more challenging or costly environment to pursue the development of new therapeutic products. Alternatively, state governments may attempt to address or react to changes at the federal level with changes to their own regulatory frameworks in a manner that is adverse to our operations. If we become negatively impacted by future governmental orders, regulations, policies or guidance as a result of the new administration, there could be a material adverse effect on us and our business.

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

We have never commercialized a product candidate for any indication. Even if our product candidates are approved by the appropriate regulatory authorities for marketing and sale, they may not gain acceptance among physicians, patients, third-party payors and others in the medical community. If any product candidate for which we obtain regulatory approval does not gain an adequate level of market acceptance, we may not generate sufficient product revenue or become profitable.

The degree of market acceptance of our product candidates, if approved, will depend on a number of factors, some of which are beyond our control, including:

- the safety, efficacy, tolerability and ease of administration of our product candidates;
- the clinical indications for which the products are approved and the approved claims that we may make for the products;
- limitations or warnings contained in the product’s approved labeling, including potential limitations on the use of the product or warnings for such products that may be more restrictive than other competitive products;
- distribution and use restrictions imposed by the FDA or comparable foreign regulatory authorities with respect to such product candidates or to which we agree as part of a mandatory REMS or risk management plan;
- changes in the standard of care for the targeted indications for such product candidates;
- the relative difficulty of administration or compliance with administration instructions of such product candidates;
- cost of treatment as compared to the clinical benefit in relation to alternative treatments or therapies;
- the availability of adequate coverage and reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid or comparable foreign programs;
- the extent and strength of our marketing and distribution of such product candidates;
- the safety, efficacy and other potential advantages of, and availability of, alternative treatments already used or that may later be approved for any of our intended indications;
- the timing of market introduction of such product candidates, as well as competitive products;
- the reluctance of physicians to switch their patients’ current standard of care;

- the reluctance of patients to switch from their existing therapy regardless of the safety and efficacy of newer products;
- our ability to offer such product candidates for sale at competitive prices;
- the extent and strength of our third-party manufacturer and supplier support;
- adverse publicity about our product or favorable publicity about competitive products; and
- potential product liability claims.

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

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

Because we have limited financial and managerial resources, we focus our development efforts on certain selected product candidates in certain selected indications. For example, we are initially focused on our most advanced product candidate, ESK-001, currently in development for the treatment of PsO and SLE, and our second product candidate, A-005, currently in development for the treatment of neuroinflammatory and neurodegenerative diseases. As a result, we may forgo or delay pursuit of opportunities with other product candidates, or other indications for our existing product candidates that later 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 current and future development programs and product candidates for specific indications may not yield any commercially viable product candidates. For example, we discontinued our proof-of-concept Phase 2a clinical trial of ESK-001 in patients with non-infectious uveitis in June 2024 based on the efficacy results of a data analysis prepared for a scheduled monitoring committee meeting, which efficacy results did not meet our clinical threshold for success despite safety results consistent with ESK-001's safety profile in psoriasis patients. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We will need to grow our organization, and we may experience difficulties in managing our growth and expanding our operations, which could adversely affect our business.

As of December 31, 2024, we had 168 full-time employees. As our development and commercialization plans and strategies develop, we expect to expand our employee base for managerial, operational, financial and other resources, including in connection with the Merger. See “—Risks Related to the Merger—Failure to attract, motivate and retain executives and other key employees could diminish the anticipated benefits of the Merger.” In addition, we have limited experience in manufacturing and commercialization. As our product candidates enter and advance through preclinical studies and clinical trials, we expect to continue to expand our development and regulatory capabilities and contract with other organizations to provide manufacturing and other capabilities for us. In the future, we expect to have to manage additional relationships with future collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our

inability to successfully manage our growth and expand our operations could adversely affect our business, financial condition, results of operations and prospects.

We are dependent on the services of our management team and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon the members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation or completion of our preclinical studies and clinical trials or the commercialization of our product candidates. Although we have executed employment agreements or offer letters with each member of our senior management team, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. We do not currently maintain “key person” life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

We will need to continue to expand and effectively manage our managerial, operational, financial and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biopharmaceutical, biotechnology and other businesses, particularly in the greater San Francisco Bay Area. If we are not able to attract, integrate, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners, CROs, CMOs and other parties. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with FDA or other regulations, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, respect our confidentiality and intellectual property rights, comply with manufacturing standards we may establish, comply with healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. If we obtain FDA approval for our product candidates and begin commercializing those products in the United States, our potential exposure under these laws will increase significantly, and our costs associated with compliance with these laws are likely to increase. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Similar requirements apply in foreign countries. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. 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 material and adverse effect on our business, financial condition, results of operations and prospects, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA or comparable foreign regulatory authorities, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid or comparable foreign programs, integrity oversight and reporting obligations, or reputational harm.

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

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets, including in the EU, the UK and Japan, for which we may rely on collaboration with third parties. We are not permitted to market or promote our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market and may never receive such regulatory approval for our product candidates. To obtain separate regulatory approval in many other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we fail to comply with the regulatory requirements in international markets and receive applicable regulatory approvals, our target market will be reduced, our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Our failure to obtain approval for our product candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that product candidate and our business, financial condition, results of operations and prospects could be adversely affected. Moreover, even if we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to these risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and reduced protection of intellectual property rights in some foreign countries.

Our business entails a significant risk of product liability and our ability to obtain sufficient insurance coverage could adversely affect our business, financial condition, results of operations and prospects.

As we conduct clinical trials of our current or future product candidates, we are exposed to significant product liability risks inherent in the development, testing, manufacturing and marketing of new treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in FDA or other regulatory authority investigation of the safety and effectiveness of our future product candidates, our manufacturing processes and facilities or our marketing programs and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension, variation or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our product candidates, termination of clinical trial sites or entire trial programs, withdrawal of clinical trial participants, injury to our reputation and significant negative media attention, significant costs to defend the related litigation, a diversion of management's time and our resources from our business operations, substantial monetary awards to trial participants or patients, loss of revenue, the inability to commercialize and products that we may develop, and a decline in our stock price. We may need to obtain higher levels of product liability insurance for later stages of clinical development or marketing of our product candidates. Any insurance we may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could adversely affect our business, financial condition, results of operations and prospects.

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

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include commercial general liability, general liability, cyber liability, workers' compensation, clinical trials and directors' and officers' liability insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our business, financial condition, results of operations and prospects.

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

We have in the past and may continue to enter into strategic transactions, including acquisitions of companies, asset purchases and in-licensing of intellectual property with the potential to acquire and advance new assets or product

candidates where we believe we are well qualified to optimize the development of promising therapies. For example, we were founded in January 2021, and subsequently acquired ESK-001 via a stock purchase of FronThera U.S. Holdings, Inc. and its wholly owned subsidiary, FronThera U.S. Pharmaceuticals LLC (the “FronThera Acquisition”). Additionally, we have entered into a Merger Agreement in connection with our planned merger with ACELYRIN. Additional potential transactions that we may consider in the future include a variety of business arrangements, including strategic partnerships, in-licensing or out-licensing of product candidates, strategic collaborations, joint ventures, restructurings, divestitures, business combinations and investments. Any such transactions, including the proposed Merger with ACELYRIN, could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. For more information regarding the risks related to the Merger, see Item 1A. “—Risks Related to the Merger.”

Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of our management. In addition, the integration of any business that we may acquire, including the ACELYRIN business, may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits of the acquisition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could adversely affect our business, financial condition, results of operations and prospects.

Our ability to use our net operating loss carryforwards and certain other tax attributes to offset taxable income or taxes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. As of December 31, 2024, we had U.S. federal net operating loss carryforwards of \$101.2 million and U.S. states net operating loss carryforwards of \$4.7 million. Under the Internal Revenue Code of 1986, as amended (the “Internal Revenue Code”), our U.S. federal net operating losses arising in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely, but the deductibility of such U.S. federal net operating losses is limited to no more than 80% of current year taxable income.

In addition, under Sections 382 and 383 of the Internal Revenue Code, if a corporation undergoes an “ownership change,” generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. As of December 31, 2024, we completed a Section 382 analysis which did not result in any expiration of U.S. federal net operating losses and credits before utilization. However, there may be ownership changes in the future, some of which may be outside of our control. If we undergo an ownership change, and our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes (if any) is limited, such limitation could harm our future results of operations by effectively increasing our future tax obligations. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use all or a material portion of our net operating losses and other tax attributes, which could adversely affect our future cash flows.

Recent and future changes to tax laws could materially adversely affect our company.

The tax regimes we are subject to or operate under, including with respect to income and non-income taxes, are unsettled and may be subject to significant change. Changes in tax laws, regulations, or rulings, or changes in interpretations of existing laws and regulations, could materially adversely affect our company. For example, the JOBS Act, the Coronavirus Aid, Relief, and Economic Security Act, and the IRA enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to such legislation may affect us, and certain aspects thereof could be repealed or modified in future legislation, possibly with retroactive effect. For example, the IRA includes provisions that will impact the U.S. federal income taxation of certain corporations, including imposing a 15% minimum tax on the book income of certain large corporations and an excise tax on certain corporate stock

repurchases that would be imposed on the corporation repurchasing such stock. In addition, many countries in Europe, as well as a number of other countries and organizations (including the Organization for Economic Cooperation and Development and the European Commission), have proposed, recommended, or (in the case of countries) enacted or otherwise become subject to changes to existing tax laws or new tax laws that could significantly increase our tax obligations in the countries where we do business or require us to change the manner in which we operate our business.

If our information technology systems, or those used by our CROs, CMOs, clinical sites or other third parties with whom we work, or our data are or were compromised, become unavailable or suffer security breaches, loss or leakage of data or other disruptions, we could suffer material adverse consequences resulting from such compromise, including but not limited to, operational or service interruption, harm to our reputation, regulatory investigations or actions, litigation, fines, penalties and liability, and other adverse consequences to our business, results of operations, and financial condition.

In the ordinary course of our business, we, and the third parties with whom we work, process personal information and other sensitive data, including intellectual property, trade secrets, proprietary or confidential business information, preclinical and clinical trial data, personal information related to relevant stakeholders, third-party data, and other sensitive data (collectively, sensitive information) and as a result, we and the third parties with whom we work face a variety of evolving threats which could cause security incidents affecting or interruptions to our information technology systems and sensitive information.

Our information technology systems and those of our CROs, CMOs, clinical sites and other third parties with whom we work are vulnerable to attack, damage and interruption from a variety of evolving threats, including but not limited to computer viruses, misconfigurations, software bugs, worms, or other vulnerabilities and malicious codes, malware (including ransomware and as a result of advanced persistent threat intrusions), application security attacks, social engineering (including through phishing attacks and deep fakes, which may be increasingly more difficult to identify as fake), supply chain attacks and vulnerabilities through our third-party service providers, denial or degradation-of-service attacks (such as credential stuffing), credential harvesting, personnel misconduct or error, fraud, server malfunctions, software or hardware failures, loss of data or other information technology assets, attacks enhanced or facilitated by AI, adware, telecommunications and electrical failures, terrorism, war, earthquakes, fires, floods, and other similar threats. Such threats are prevalent, are occurring more often, are increasingly difficult to detect, and come from a variety of sources, including traditional computer “hackers,” threat actors, “hacktivists,” organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors. In particular, ransomware attacks, including those from organized criminal threat actors, nation-states and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, loss of data (including sensitive information), loss of income, significant extra expenses to restore data or systems, reputational loss, the diversion of funds and other consequences. To alleviate the negative impact of a ransomware attack, it may be preferable to make extortion payments, but we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments).

Some actors also now engage and are expected to continue to engage in cyberattacks, including without limitation nation-state actors, for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, and the third parties with whom we work, may be vulnerable to a heightened risk of these attacks, including retaliatory cyberattacks, that could materially disrupt our systems, operations and supply chain. In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive data about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

Additionally, remote work has become more common and has increased risks to our information technology systems and data, as more of our personnel utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations.

Furthermore, future or past business transactions (such as the proposed Merger or other acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities’ systems and technologies. Additionally, we may discover security

issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate acquired entities into our information technology environment and security program.

We have in the past and may in the future expend significant resources and modify our business activities to try to protect against security incidents. While we take steps designed to anticipate, detect and remediate threats and vulnerabilities, because the threats and techniques used to exploit such vulnerabilities and gain unauthorized access to, to sabotage or otherwise compromise systems change frequently, are often sophisticated in nature, and are often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement and maintain adequate preventative measures. Therefore, such vulnerabilities have and could be exploited but may not be detected until after a security incident has occurred. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities and we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. There can be no assurance that our information security policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems and sensitive information.

Our reliance on third-party service providers could introduce additional cybersecurity risks and vulnerabilities, including supply-chain attacks and other threats to our business operations. We rely on third-party service providers and technologies to operate critical business systems and to process sensitive information in a variety of contexts, including, without limitation, cloud-based infrastructure, data hosting, encryption and authentication technology, personnel email, human resource management, training and other functions. We also rely on third-party service providers to assist with our clinical trials or otherwise to operate our business, including to manage and store sensitive patient data from our clinical trials. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. Our third-party service providers have and may in the future experience a security incident or other interruption. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain or our third-party partners' supply chains have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third-party information technology systems that support our operations.

We and certain of our service providers have been and are from time to time subject to cyberattacks and security incidents. Any of the previously identified or similar threats have or could cause a security incident or other interruption that resulted or results in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure, or other processing of, or access to our sensitive information or our information technology systems, or those of the third parties with whom we work. A security incident or other interruption could disrupt our ability (and that of third parties with whom we work) to conduct clinical trials. Additionally, sensitive information of the company could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel's, or vendors' use of generative AI technologies.

The costs related to significant security breaches or disruptions could be material and cause us to incur significant expenses. If the information technology systems of our CROs, CMOs, clinical sites and other third parties become subject to disruptions or security incidents, 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. Further, our cyber liability insurance coverage may not be sufficient to cover the financial, legal, business reputational or other losses that may result from an interruption or breach.

Security incidents have and could result in a disruption of our business and development programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for a product candidate could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data, or may limit our ability to effectively execute a product recall, if required in the future. To the extent that any disruption or security incident were to result in the loss of or damage to our data or applications, or inappropriate disclosure of sensitive information, we could incur liability and the further development of any product candidates could be delayed.

Applicable data privacy and security obligations may require us, or we may voluntarily choose, to notify relevant stakeholders, including affected individuals, regulators, and investors, of security incidents, or take other actions, such as providing credit monitoring and identity theft protection services. Such disclosures and related actions can be costly, and the disclosure or the failure to comply with such applicable requirements could lead to adverse consequences.

Security incidents (or perceived security incidents), may result in material adverse consequences such as legal claims or proceedings, liability including litigation exposure, penalties and fines under relevant legal obligations, enforcement actions and investigations by regulatory authorities, additional reporting requirements or oversight, restrictions on processing sensitive information (including personal information), indemnification obligations, monetary fund diversions, diversion of management attention, other financial loss, and damage to our reputation and a loss of confidence in us and our ability to conduct clinical trials, which could delay the clinical development of our product candidates, and of which may adversely affect our business, results of operations or financial condition.

Our operations are concentrated in one location, and we or the third parties upon whom we depend may be adversely affected by a wildfire, earthquake or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our current operations are predominantly located in California. Any unplanned event, such as flood, wildfire, explosion, earthquake, extreme weather condition, medical epidemic including the COVID-19 pandemic, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Any similar impacts of natural or manmade disasters on our third-party service providers, such as our CMOs and CROs located globally, could cause delays in our clinical trials and may have a material and adverse effect on our ability to operate our business and have significant negative consequences on our financial and operating conditions. If a natural disaster, power outage or other event occurred that prevented us from using our clinical trial sites, impacted clinical supply or the conduct of our clinical trials, that damaged critical infrastructure, such as the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans that we and third parties upon whom we rely have or may have in place may prove inadequate in the event of a serious disaster or similar event. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our CMOs, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our development programs may be harmed. Any business interruption could adversely affect our business, financial condition, results of operations and prospects.

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

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

even if we obtain significant market share for our product candidates, because some of our potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Our cash and cash equivalents may be exposed to failure of our banking institutions.

While we seek to minimize our exposure to third-party losses of our cash and cash equivalents, we hold our balances in a number of large financial institutions. Notwithstanding, those institutions are subject to risk of failure. For example, on March 10, 2023, Silicon Valley Bank (“SVB”) was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (the “FDIC”) as receiver. Similarly, on March 12, 2023, Signature Bank was also swept into receivership. The U.S. Department of Treasury, the Federal Reserve Board (the “Federal Reserve”), and the FDIC released a statement that indicated that all depositors of SVB would have access to all of their funds, including funds held in uninsured deposit accounts, after only one business day of closure. The U.S. Department of Treasury, the FDIC and the Federal Reserve have announced a program to provide up to \$25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. There is no guarantee, however, that the U.S. Department of Treasury, the FDIC and the Federal Reserve will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we expect to assess our banking relationships as we believe necessary or appropriate, our access to cash in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the financial institutions with which we have banking relationships, and in turn, us.

These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could also include factors involving financial markets or the financial services industry generally. The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; or termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

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

In addition, one or more of our critical vendors, third party manufacturers, or other business partners could be adversely affected by any of the liquidity or other risks that are described above, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. Any business partner bankruptcy or insolvency, or any breach or default by a business partner, or the loss of any significant supplier relationships, could result in material adverse impacts on our current and/or projected business operations and financial condition.

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

Public perception may be influenced by claims, such as claims that our product candidates are unsafe, unethical or immoral and, consequently, our approach may not gain the acceptance of the public or the medical community. Adverse public attitudes may also adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing, and their patients being willing to receive, treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. AEs in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in withdrawal of clinical trial participants, increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. In addition, side effects generally associated with TYK2 or JAK inhibitors may negatively impact public perception of us or ESK-001 and A-005. More restrictive government regulations or negative public opinion could have an adverse effect on our business, financial condition, results of operations and prospects, and may delay or impair the development and, if approved, commercialization of our product candidates or demand for any products we may develop.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates and any future product candidates we may develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, and our ability to successfully develop and commercialize our product candidates may be adversely affected.

We rely upon a combination of patents, know-how and confidentiality agreements to protect the intellectual property related to our product candidates and technologies and to prevent third parties from copying and surpassing our achievements, thus eroding our competitive position in our market. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries for our product candidates and their uses, as well as our ability to operate without infringing, misappropriating or otherwise violating the proprietary rights of others. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates and novel discoveries that are important to our business. Our pending and future patent applications may not result in patents being issued. We cannot assure you that issued patents will afford sufficient protection of our product candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive products or product candidates.

Obtaining and enforcing patents is expensive and time-consuming, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications or maintain and/or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner. We may not be able to obtain or maintain patent applications and patents due to the subject matter claimed in such patent applications and patents being in disclosures in the public domain. It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we have in the past and will continue to enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CMOs, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we may not be able to prevent any third parties from using any of our technology that is in the public domain to compete with our product candidates.

Composition of matter patents for pharmaceutical product candidates often provide a strong form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. However, we cannot be certain that the claims in our pending patent applications directed to composition of matter of our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any

of our issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product candidates for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, clinicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. As a result, the issuance, scope, validity, enforceability and commercial value of any patent rights are highly uncertain. Our pending and future owned or in-licensed patent applications may not result in issued patents that protect our product candidates effectively to prevent others from commercializing our product candidates or otherwise provide any competitive advantage. In fact, patent applications may not issue as patents at all. The coverage claimed in a patent application can also be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and our pending patent applications may be challenged in patent offices in the United States and abroad. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. For example, our pending patent applications may be subject to third-party pre-issuance submissions of prior art to the USPTO, or our issued patents may be subject to post-grant review (“PGR”) proceedings, oppositions, derivations, reexaminations, interferences, inter partes review (“IPR”) proceedings or other similar proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. Such submissions may also be made prior to a patent’s issuance, precluding the granting of a patent based on one or more of our owned pending patent applications. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of our product candidates. Such challenges also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Any of the foregoing could adversely affect our business, financial condition, results of operations and prospects.

A third party may also claim that our patent rights are invalid or unenforceable in a litigation. An adverse result in any legal proceeding could put one or more of our owned or patents at risk of being invalidated or interpreted narrowly and could allow third parties to commercialize our products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize our technology, products or product candidates without infringing third-party patent rights.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such candidates are commercialized. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Any failure to obtain or maintain patent protection with respect to our product candidates or their uses could adversely affect our business, financial condition, results of operations and prospects.

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

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any potential future licensors or collaborators will be successful in protecting our product candidates by obtaining and

defending patents. We have several pending United States and foreign patent applications in our portfolio. We cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- whether the patent applications that we own will result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries; or
- whether, if the COVID-19 pandemic continues to spread around the globe, we may experience patent office interruption or delays to our ability to timely secure patent coverage to our product candidates.

We cannot be certain that the claims in our or any future licensors' pending patent applications directed to our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries. There can be no assurance that any such patent applications will issue as granted patents. One aspect of the determination of patentability of our or any future licensors' inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our or any future licensors' patent claims or, if issued, affect the validity or enforceability of a patent claim. Even if the patents do issue based on our or any future licensors' patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our or any future licensors' portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our product candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

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

Patents are of national or regional effect, and filing, prosecuting and defending patents on all of our research programs and product candidates in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our or any future licensors' inventions in all countries outside the United States, even in jurisdictions where we or any future licensors do pursue patent protection, or from selling or importing products made using our or any future licensors' inventions in and into the United States or other jurisdictions. Competitors may use our or any future licensors' 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 or any future licensors have patent protection, but enforcement is not as strong as that in the United States. These competitor products may compete with our product candidates, and our or any future licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

Certain countries outside the United States have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. As a result, a patent owner may have limited remedies in certain circumstances, which could materially diminish the value of such patent. If we or any future licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license in the future.

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

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

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

- others may be able to make product candidates that are similar to ours but that are not covered by the pending patent applications that we own or any patents or patent applications that we may in-license in the future;
- we or any future licensors or collaborators might not have been the first to make the inventions covered by the pending patent application that we own or may in-license in the future;
- we or any future licensors or collaborators might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing or otherwise violating our owned intellectual property rights or any patent applications that we may license in the future;
- it is possible that noncompliance with the USPTO and foreign governmental patent agencies requirement for a number of procedural, documentary, fee payment and other provisions during the patent process can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- it is possible that our pending owned patent applications or those that we may own or license in the future will not lead to issued patents;
- issued patents, if any arise in the future, that we either own or that we may license in the future may be revoked, modified, or held invalid or unenforceable, as a result of legal challenges by our competitors;
- others may have access to the same intellectual property rights licensed to us in the future on a non-exclusive basis;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- we cannot predict the scope of protection of any patent issuing based on our or any future licensors' patent applications, including whether the patent applications that we own, or, in the future, in-license will result in issued patents with claims directed to our product candidates or uses thereof in the United States or in other foreign countries;
- there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates; the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents, if they issue in the future, are valid, enforceable and infringed;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patent applications.

Should any of these or similar events occur, they could significantly harm our business, financial condition, results of operations and prospects.

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

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. There can be no assurance that our operations do not, or will not in the future, infringe, misappropriate or otherwise violate existing or future third-party patents or other intellectual property rights. Identification of third-party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

Numerous United States and foreign patents and pending patent applications exist in our market that are owned by third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or

may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. We do not always conduct independent reviews of pending patent applications and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain United States applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These patent applications may later result in issued patents, or the revival of previously abandoned patents, that may be infringed by the manufacture, use or sale of our product candidates or will prevent, limit or otherwise interfere with our ability to make, use or sell our product candidates.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

We cannot provide any assurances that third-party patents and other intellectual property rights do not exist which might be enforced against our current technology, including our research programs, product candidates, their respective methods of use, manufacture and formulations thereof, and could result in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

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

Competitors or other third parties may infringe our patents, trademarks or other intellectual property. To counter infringement or unauthorized use, we or any future licensors may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Our or any future licensors' pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents or any future licensors' patents are invalid or unenforceable, or both. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, insufficient written description or failure to claim patent-eligible subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours or any future licensors 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 or any future licensors' patent claims do not cover the invention, or decide that the other party's use of our or any future licensors' patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). An adverse outcome in a litigation or proceeding involving our or any future licensors' patents could limit our ability to assert our or any future licensors' 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 position, and our business, financial condition, results of operations and prospects. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have

asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

We may become involved in third-party claims of intellectual property infringement, which may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation involving the infringement of patents and other intellectual property rights in the biotechnology and pharmaceutical industries. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights and who allege that our product candidates, uses and/or other proprietary technologies infringe their intellectual property rights. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk that our product candidates may give rise to claims of infringement of the patent rights of others increases. Moreover, it is not always clear to industry participants, including us, which patents exist which may be found to cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications currently pending in our fields, there may be a risk that third parties may allege they have patent rights which are infringed by our product candidates, technologies or methods.

If a third party alleges that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property misappropriation which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement or misappropriation, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds we have willfully infringed intellectual property rights, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- an injunction prohibiting us from manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party agrees to license its patent rights to us;
- even if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights protecting our products; and
- we may be forced to try to redesign our product candidates or processes so they do not infringe third-party intellectual property rights, an undertaking which may not be possible or which may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of

any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting preclinical and clinical trials and other development activities in the United States is not considered an act of infringement. While we may believe that patent claims or other intellectual property rights of a third party would not have a materially adverse effect on the commercialization of our product candidates, we may be incorrect in this belief, or we may not be able to prove it in litigation. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is “clear and convincing,” a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates.

Patent applications can take many years to issue. There may be currently pending patent applications which may later result in issued patents that may be infringed by our product candidates. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents, held now or obtained in the future by a third party, were found by a court of competent jurisdiction to cover the manufacturing process of our product candidates, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover any aspect of our formulations, any combination therapies or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates, if approved, may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys’ fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

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

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates on commercially reasonable terms or at all. Even if we are able to in-license any such necessary intellectual property, it could be on nonexclusive terms, thereby giving our competitors and other third parties access to the same intellectual property licensed to us, and it could require us to make substantial licensing and royalty payments. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization

capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have obtained, we may have to abandon development of the relevant program or product candidate, which could adversely affect our business, financial condition, results of operations and prospects.

We may enter into license agreements in the future with others to advance our existing or future research or allow commercialization of our existing or future product candidates, if approved. These licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and product candidates in the future. In that event, we may be required to expend significant time and resources to redesign our product candidates, or the methods for manufacturing them, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, if approved, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current manufacturing methods, product candidates, or future methods or product candidates resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

We may become subject to claims challenging the inventorship or ownership of our or any future licensors' patents and other intellectual property.

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

Any future licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the United States government, such that these licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could adversely affect our competitive position, business, financial condition, results of operations and prospects.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could adversely affect our business, financial condition, results of operations and prospects.

We may form or seek collaborations or strategic alliances or enter into licensing arrangements in the future, and we may neither enter into, nor realize the benefits of, such alliances or licensing arrangements.

Any future collaborations that we enter into may not be successful and we may not enter into such collaborations at all. The success of our collaboration arrangements will depend heavily on the efforts and activities of any future collaborators. Collaborations are subject to numerous risks, which may include that:

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

If we fail to comply with our obligations in agreements under which we in-license or acquire development or commercialization rights to product candidates, or data from third parties, we could lose such rights that are important to our business.

We may in the future in-license or otherwise acquire development or commercialization rights to product candidates or data from third parties, and any future licensors may rely upon third-party companies, consultants or collaborators, or on funds from third parties such that licensors are not the sole and exclusive owners of the patents we in-license. If any future licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize future product candidates that may be subject of such licensed rights could be adversely affected. In spite of our efforts, any future licensors might conclude that we are in material breach of obligations under our license agreements and may therefore have the right to terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered

by such license agreements. If such in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, our competitors will have the freedom to seek regulatory approval of, and to market, products identical to our product candidates and the licensors to such in-licenses could prevent us from developing or commercializing product candidates that rely upon the patents or other intellectual property rights which were the subject matter of such terminated agreements. Any of these events could adversely affect our business, financial condition, results of operations, and prospects.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- our financial or other obligations under the license agreement;
- the extent to which our processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those obligations;
- the inventorship or ownership of inventions and know-how resulting from the joint creation or use of intellectual property by any future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, any 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 our rights to the relevant intellectual property or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could adversely affect our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we may license in the future prevent or impair our ability to maintain future licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could adversely affect our business, financial condition, results of operations, and prospects.

Any license agreements we enter into in the future may be subject to certain rights retained by third parties.

Any future licensors may retain certain rights under the relevant agreements with us, including the right to use the underlying product candidates for academic and research use, to publish general scientific findings from research related to the product candidates, to make customary scientific and scholarly disclosures of information relating to the product candidates, or to develop or commercialize the licensed product candidates in certain regions.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act (the “Bayh-Dole Act”). The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. We may at times choose to collaborate with academic institutions to accelerate our preclinical research or development. While we do not currently engage, and it is our policy to avoid engaging, university partners in projects in which there is a risk that federal funds may be commingled, we cannot be sure that any co-developed intellectual property will be free from government rights pursuant to the Bayh-Dole Act. Although none of our licenses to date are subject to march-in rights, if, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with

federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining, defending, maintaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, and may diminish our ability to protect our inventions, obtain, maintain, enforce and protect our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our future owned and licensed patents. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (the “Leahy-Smith Act”), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of patent applications filed after March 2013 and the enforcement or defense of our future issued patents or claiming priority to patent applications filed after March 2013. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include 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. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including PGR, IPR, and derivation proceedings.

Further, because of a lower evidentiary standard in these USPTO post-grant proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our or any future licensors’ patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or any future licensors’ patent applications and the enforcement or defense of our or any future licensors’ future issued patents, all of which could adversely affect our business, financial condition, results of operations and prospects.

After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours or any future licensors even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or any future licensors were the first to either (i) file any patent application related to our product candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or any future licensors’ patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future issued patents, all of which could adversely affect our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Depending on future actions by the United States 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 unpredictable

ways that would weaken our or any future licensors' ability to obtain new patents and patents that we or any future licensors might obtain in the future. We cannot predict how future decisions by the courts, the United States Congress or the USPTO may impact the value of our patents. Any similar adverse change in the patent laws of other jurisdictions could also adversely affect our business, financial condition, results of operations and prospects.

In 2012, the European Union Patent Package ("EU Patent Package") regulations were passed with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court ("UPC") for litigation involving European patents. The EU Patent Package was implemented on June 1, 2023. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. Our European patent applications, if issued, could be challenged in the UPC. During the first seven years of the UPC's existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. We may decide to opt out our future European patents from the UPC, but doing so may preclude us from realizing the benefits of the UPC. Moreover, if we do not meet all of the formalities and requirements for opt-out under the UPC, our future European could remain under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunction. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated as a result of noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and patent applications. We rely on our outside patent counsel to pay these fees due to United States and non-United States patent agencies. The USPTO and various non-United States government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could adversely affect our business, financial condition, results of operations and prospects.

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

Patents have a limited lifespan. 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 or international patent application 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 products or product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of products or new product candidates, patents protecting such products or candidates might expire before or shortly after such products or candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient and continuing rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA regulatory approval of our product candidates, one or more of our issued United States patents or issued United States patents that we may own in the future may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 (the "Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for

patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under SPC. However, we may not be granted any extensions for which we apply because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. Moreover, the applicable time period or the scope of patent protection afforded 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, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents, we seek to rely on trade secret protection to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that is not covered by our patents. We may not be able to meaningfully protect our trade secrets. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed to our competitors or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws within the United States. We may need to share our trade secrets and proprietary know-how with current or future partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

Monitoring and detecting unauthorized disclosure or other compromise of trade secrets is difficult, and we do not know whether the steps we have taken to prevent such compromise are, or will be, adequate. If we were to enforce a claim that a third party had illegally obtained and was using our trade secrets, it would be expensive and time-consuming, and the outcome would be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. For example, significant elements of our business, including confidential aspects of sample preparation, methods of manufacturing, proprietary assays, computational-biological algorithms, data analytics and machine learning related to genetics, genomics, proteomics, biomarkers and samples, and related processes and software, are based on unpatented trade secrets, including those of our collaborators. For example, our collaborator, Foresite Labs, utilizes extensive trade secret algorithms, machine learning and AI analysis techniques, and we rely on their maintenance of these trade secrets. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors have in the past and may in the future be employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. An inability to incorporate such technologies or features would harm our business and may prevent us from successfully commercializing our technologies or product candidates. In addition, we may lose personnel as a result of such claims and any such litigation, or the threat thereof, may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our technologies, or product candidates, which could adversely affect our business, financial condition, results of operations and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our patents or patent applications. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technologies and product candidates. Such challenges may also result in our inability to develop, manufacture or commercialize our technologies and product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technologies and product candidates. Any of the foregoing could adversely affect our business, financial condition, results of operations and prospects.

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

Our unregistered trademarks, trade names or future registered trademarks may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we are given an opportunity to respond to such rejections, we may be unable to overcome them. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, which may not survive such proceedings. Moreover, any name we have proposed to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or an equivalent administrative body in a foreign jurisdiction objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then

we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain name or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Government Regulation

Even if we receive regulatory approval for our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal. We may also be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Any regulatory approvals that we or our future collaborators obtain for our product candidates may also be subject to limitations on the approved indicated uses for which a product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance to monitor the safety and efficacy of the product candidate.

In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, post-approval monitoring and AE reporting, storage, import, export, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. The FDA has significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The FDA also has the authority to require a REMS after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. Comparable foreign regulatory authorities may have similar authority. The manufacturing facilities we use to make a future product, if any, will also be subject to periodic review and inspection by the FDA and other regulatory authorities, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. As we expect to rely on third-party manufacturers, we will have limited control over compliance with applicable rules and regulations by such manufacturers.

In addition, any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. For example, the FDA and comparable foreign regulatory authorities impose stringent restrictions on manufacturers' communications regarding use of their products. Although clinicians may prescribe products for off-label uses, as the FDA and comparable foreign regulatory authorities do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, the FDA and such comparable foreign regulatory authorities do restrict promotional communications from companies or their sales force with respect to off-label uses of products. Specifically, any regulatory approval that the FDA grants is limited to those specific diseases and indications for which a product is deemed to be safe and effective by FDA, and our ability to promote any products will be narrowly limited to those indications that are specifically approved by the FDA. Similar restrictions apply in other countries. In the EU, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics ("SmPC") which may require approval by the competent national authorities in connection with a marketing authorization. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU. If we are found to have promoted such off-label uses, we may become subject to significant liability. In addition, if we do not conduct head-to-head comparative clinical trials for our product candidates, we will be unable to make comparative claims regarding any other products in the promotional materials for our product candidates. If we promote our products, if approved, in a manner inconsistent with FDA-approved labeling, or the labeling approved by another comparable foreign regulatory authority, or otherwise not in compliance with FDA regulations or comparable foreign rules, we may be subject to enforcement action. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Subsequent discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure by us, our contract manufacturers or service providers, or collaborators to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- operating restrictions;
- holds on clinical trials;
- warning or untitled letters;
- refusal by the FDA or comparable foreign regulatory authorities to approve, or delays in the approval of, pending applications or supplements to approved applications;
- suspension, variation or revocation of product approvals;
- product seizure or detention or refusal to permit the import or export of products; and
- injunctions, fines or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

The FDA's and comparable foreign regulatory authorities' policies may change and additional government regulations may be promulgated that could prevent, limit or delay marketing authorization of any product candidates we develop. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. In addition, the U.S. Supreme Court's July 2024 decision to overturn established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. As a result of the U.S. Supreme Court's decision, the FDA and other agencies may be less inclined to engage in formal regulation and may rely to a greater degree on informal guidance, which may not always be susceptible to immediate challenge. We cannot predict the likelihood, nature or extent of government regulation or guidance that may arise from future court decisions, legislation, or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Recently enacted legislation, future legislation and other healthcare reform measures may increase the difficulty and cost for us to obtain regulatory approval for and commercialize our product candidates and may affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain regulatory approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “ACA”) was enacted in the United States, which made a number of substantial changes in the way healthcare is financed by both governmental and private insurers. The ACA included a number of provisions that may reduce the profitability of drug products, including provisions intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, the American Taxpayer Relief Act of 2021, effective January 1, 2024, eliminated the statutory cap on rebate amounts owed by drug manufacturers under the Medicaid Drug Rebate Program, which was previously capped at 100% of the Average Manufacturer Price for a covered outpatient drug.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Healthcare reform initiatives culminated in the enactment of the IRA in August 2022, which, among other things, allows HHS to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that the Centers for Medicare & Medicaid Services reimburses under Medicare Part B and Part D. Only high-expenditure single-source drugs that have been approved for at least 7 years for single-source drugs (11 years for biologics) are eligible to be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. CMS selected the Medicare Part D products in 2023, negotiations began in 2024, and the negotiated maximum fair price for each product has been announced. These negotiations resulted in significant price reductions for the products from their 2023 list prices, ranging from 38 to 79 percent, with an average price reduction of 59.4 percent. The price cap for each of these products, which cannot exceed a statutory ceiling price, will take effect in 2026. Negotiations for Medicare Part B products will begin in 2026 with the negotiated price taking effect in 2028.

A drug or biological product that has an orphan drug designation for only one rare disease or condition are excluded from the IRA’s price negotiation requirements, but will lose that exclusion if it receives designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The negotiated prices have represented, and will continue to represent, a significant discount from average prices to wholesalers and direct purchasers. The law also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation, and in November 2024, CMS finalized regulations for the Medicare Part B and Part D inflation rebates. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the pharmaceutical industry.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, restrictions on certain product access, reporting on price increases and the introduction of high-cost drugs. In some states, laws have been enacted to encourage importation of lower cost drugs from other countries and bulk purchasing. For example, the FDA released a final rule in September 2020 providing guidance for states to build and submit proposals for importing drugs from Canada, and FDA authorized the first such plan in Florida in January 2024, which has been extended until July 6, 2025. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted proposals that are pending review by the FDA. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drug products that we successfully commercialize or put pressure on our product pricing.

We expect that the ACA, the IRA, and any 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. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost-containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved.

Moreover, in order to obtain reimbursement for our products in some European countries, including some EU member states, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. This of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU member states. In December 2021, Regulation No 2021/2282 on HTA amending Directive 2011/24/EU, was adopted in the EU. While the HTA 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 EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU member states for product candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected.

Our operations and relationships with healthcare providers, healthcare organizations and third-party payors will be subject to applicable anti-bribery, anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to, among other things, enforcement actions, criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Our future arrangements with healthcare providers, healthcare organizations and third-party payors will expose us to broadly applicable anti-bribery, fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our product candidates, if approved. Restrictions under applicable federal, state and foreign anti-bribery and healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, 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 and state healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal criminal and civil false claims laws, including the federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions against individuals or entities, and the Federal Civil Monetary Penalties Laws, which prohibit, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, knowingly making, using or causing to be

made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Moreover, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;

- HIPAA, which imposes criminal and civil liability, prohibits, among other things, knowingly and willfully executing, or attempting to execute a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of covered drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with certain exceptions, to report annually to CMS information on certain payments and other transfers of value to clinicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), teaching hospitals, and certain other health care providers (such as physician assistants and nurse practitioners), as well as ownership and investment interests held by the clinicians described above and their immediate family members;
- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof;
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback and false claims laws, that 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
- certain state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the government in addition to requiring drug manufacturers to report information related to payments to clinicians and other healthcare providers or marketing expenditures and drug pricing information, and state and local laws that require the registration of pharmaceutical sales representatives.

In the EU, interactions between pharmaceutical companies and healthcare professionals and healthcare organizations are governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and in the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of pharmaceutical products is prohibited in the EU. Relationships with healthcare professionals and associations are subject to stringent anti-gift statutes and anti-bribery laws, the scope of which differs across the EU. In addition, national transparency and reporting rules may require pharmaceutical companies to report/publish transfers of value provided to healthcare professionals and associations on a regular (e.g. annual) basis.

If we or our future collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our product candidates successfully and could harm our reputation and lead to reduced acceptance of our products, if approved by the market.

Efforts to ensure that our current and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving

applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any such requirements, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA or comparable foreign regulatory authorities, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid or comparable foreign programs, integrity oversight and reporting obligations, or reputational harm, any of which could adversely affect our financial results. These risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

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

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a study that compares the cost-effectiveness of our product candidate to other available therapies. In addition, many countries outside the United States have limited government support programs that provide for reimbursement of drugs such as our product candidates, with an emphasis on private payors for access to commercial products. If reimbursement of our products, if approved is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, rules; contractual obligations; policies; and other obligations related to data privacy and security. Our (including the third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse consequences for our business, results of operations and financial condition.

In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process or processing) personal information and other sensitive information, including proprietary and confidential business data, trade secrets, employee data, intellectual property, data we collect about trial participants in connection with clinical trials, and other sensitive third-party data (collectively, sensitive information). Our data processing activities presently and may in the future subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

Various federal, state, local and foreign legislative and regulatory bodies, or self-regulatory organizations, may expand current laws, rules or regulations, enact new laws, rules or regulations or issue revised rules or guidance regarding data privacy and security. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal information privacy laws, and consumer protection laws. For example, HIPAA imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. We may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA.

Additionally, the California Consumer Privacy Act ("CCPA") applies to personal information of California consumers, business representatives, and employees, and among other things requires regulated businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights, including the

right to opt out of certain disclosures of their information. The CCPA provides for civil penalties as well as a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. In addition, although the CCPA includes limited exceptions, including for certain information collected as part of clinical trials, the CCPA may impact our processing of personal data and our compliance costs depending on how it is interpreted. Similar laws are being considered or have been enacted in several other states, as well as at the federal and local levels. While U.S. state privacy laws, like the CCPA, may also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties with whom we work. In addition to government activity, privacy advocacy groups and technology and other industries are considering various new, additional or different self-regulatory standards that may place additional burdens on us.

There are also various laws, regulations and industry standards in other jurisdictions outside the United States relating to data privacy and security, with which we presently or in the future may need to comply. For example, the EU's General Data Protection Regulation ("EU GDPR") and the UK's equivalent ("UK GDPR"), collectively, GDPR, impose strict requirements for processing personal information (referred to as "personal data" under the GDPR). Notably, under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to €20 million under the EU GDPR / £17.5 million under the UK GDPR, or, in each case, 4% of the annual global revenue of the noncompliant undertaking, whichever is greater. The GDPR also provides for private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. Additionally, EU member states may introduce further conditions, including limitations, and make their own laws and regulations further limiting the processing of "special categories of personal data," including personal data related to health, biometric data used for unique identification purposes and genetic information, which could limit our ability to process such special categories of personal data, and could cause our compliance costs to increase, ultimately adversely affecting our business, financial condition, results of operations and prospects.

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

In addition, we may be unable to transfer personal information from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal information to other countries. In particular, the European Economic Area (the "EEA") and the UK have significantly restricted the transfer of personal information to the United States and other countries whose privacy laws it generally believes are inadequate. Although there are currently various mechanisms that may be used to transfer personal information from the EEA and UK to the United States in compliance with law, such as the EEA standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, the EU-US Data Privacy Framework, and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal information to the United States.

Other jurisdictions may adopt or have already adopted similarly stringent data localization and cross-border data transfer laws. If there is no lawful manner for us to transfer personal information from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal information necessary to operate our business. Additionally, companies that transfer personal information out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the

GDPR's cross-border data transfer limitations. Regulators in the United States are also increasingly scrutinizing certain personal information transfers and have enacted certain restrictions on cross-border personal information transfers.

In addition to data privacy and security laws, we are also bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful.

Each of these laws, rules, regulations and contractual obligations relating to data privacy and security, and any other such changes or new laws, rules, regulations or contractual obligations could impose significant limitations, require changes to our business, or restrict our collection, use, storage or processing of personal information, which may increase our compliance expenses and make our business more costly or less efficient to conduct. In addition, any such changes could compromise our ability to develop an adequate marketing strategy and pursue our growth strategy effectively or even prevent us from providing certain products in jurisdictions in which we currently operate and in which we may operate in the future or incur potential liability in an effort to comply with such legislation, which, in turn, could adversely affect our business, financial condition, results of operations and prospects. Complying with these numerous, complex and often changing regulations is expensive and difficult, and failure to comply with any data privacy or security laws, whether by us, one of our CROs, CMOs or another third party with whom we work, could adversely affect our business, financial condition, results of operations and prospects, including but not limited to: regulatory investigation costs; material fines and penalties; compensatory, special, punitive and statutory damages; litigation (including class claims); consent orders regarding our data privacy and security practices; requirements that we provide notices, bans on processing personal information (including clinical trial data), orders to destroy or not use personal information, credit monitoring services and/or credit restoration services or other relevant services to impacted individuals in the event of an information security incident impacting personal information; adverse actions against our licenses to do business; reputational damage; and injunctive relief. The implementation of the GDPR has increased our responsibility and liability in relation to sensitive information that we process, including in clinical trials, that is subject to the GDPR, and we may be required to put in place additional mechanisms to comply with the GDPR and other applicable laws and regulations, which could divert management's attention and increase our cost of doing business. In addition, new regulation or legislative actions regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. For instance, in Europe, the second Network and Information Security Directive ("NIS2") aims to improve the resilience and incident response capabilities of entities operating in a number of sectors, including the health sector. Non-compliance with NIS2, as applicable to us, may lead to administrative fines of a maximum of €10 million or up to 2% of the total worldwide turnover of the preceding financial year. In this regard, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy, data protection and security in the United States, the EEA, the UK and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties with whom we work may fail to comply with such obligations, which could negatively impact our business operations. Any actual or perceived failure by us or third parties with whom we work to comply with any federal, state or foreign laws, rules, regulations, industry self-regulatory principles, industry standards or codes of conduct, regulatory guidance, orders to which we (or third parties with whom we work) may be subject or other legal obligations relating to privacy, data protection, data security or consumer protection could adversely affect our reputation, brand and business. We may also be contractually required to indemnify and hold harmless third parties from the costs or consequences of non-compliance with any laws, rules and regulations or other legal obligations relating to privacy or any inadvertent or unauthorized use or disclosure, or other compromise of data that we store or handle as part of operating our business. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: interruptions or stoppages in our business operations (including clinical trials and the development of product candidates); inability to process personal information or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations.

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

We also publicly post privacy policies, marketing materials, whitepapers, and other statements concerning data privacy, security, and our collection, use, disclosure and other processing of the personal information provided to us or that we collect. Although we endeavor to comply with our public statements and documentation, we may at times fail to do so or be perceived to have failed to do so. Regulators in the United States and elsewhere are increasingly scrutinizing these statements, and our publication of our privacy policies and other statements we publish that provide promises and assurances about data privacy and security can subject us to potential claims if they are found to be deceptive, unfair, misleading, or misrepresentative of our actual practices. Any actual or perceived failure by us to comply with federal, state or foreign laws, rules or regulations, industry standards, contractual or other legal obligations, or any actual, perceived or suspected cybersecurity incident, whether or not resulting in unauthorized access to, or acquisition, release, transfer or other compromise of personal information or other sensitive information, may result in enforcement actions and prosecutions, private litigation (including class action claims), significant fines, penalties (including bans on processing personal information or orders to destroy or not use personal information) and censure, claims for damages by affected individuals, regulatory inquiries and investigations or adverse publicity and could cause reputational harm, any of which could adversely affect our business, financial condition, results of operations and prospects. The successful assertion of one or more large data privacy or security claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

Risks Related to Our Reliance on Third Parties

We may have conflicts with any future licensors or collaborators that could delay or prevent the development or commercialization of our product candidates.

We may enter into strategic transactions in the future, and we may have conflicts with any potential licensors or collaborators, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our future collaborators, such collaborator may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating revenue: disputes regarding milestone payments or royalties; uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into future additional collaborations; unwillingness by such collaborator to cooperate in the development or manufacture of a product candidate, including providing us with data or materials; unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities; initiating of litigation or alternative dispute resolution options by either party to resolve the dispute; or attempts by either party to terminate the agreement.

We have relied and expect to continue to rely on third parties to conduct our preclinical studies and clinical trials. If those third parties do not perform as contractually required, fail to satisfy legal or regulatory requirements, miss expected deadlines or terminate the relationship, our development programs could be delayed, more costly or unsuccessful, and we may never be able to seek or obtain regulatory approval for or commercialize our product candidates.

We rely and intend to rely in the future on third-party clinical investigators, CROs and clinical data management organizations to conduct, supervise and monitor preclinical studies and clinical trials of our current or future product candidates. Because we currently rely and intend to continue to rely on these third parties, we will have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would have had we conducted them independently. These parties are not, and will not be, our employees and we will have limited control over the amount of time and resources that they dedicate to our programs. Additionally, such parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs.

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

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

Our reliance on these third parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable trial protocol and legal, regulatory and scientific standards, and our reliance on the CROs, clinical trial sites, and other third parties does not relieve us of these responsibilities. For example, we will remain responsible for ensuring that each of our preclinical studies are conducted in accordance with good laboratory practices, where applicable, and clinical trials are conducted in accordance with GCPs and applicable rules. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections (including through inspections that may be conducted once we submit an NDA to the FDA) of trial sponsors, clinical investigators, trial sites and certain third parties including CROs. If we, our CROs, clinical trial sites, or other third parties fail to comply with applicable GCP or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. Moreover, our business may be significantly impacted if our CROs, clinical investigators or other third parties violate federal or state healthcare fraud and abuse or false claims laws and regulations or healthcare privacy and security laws, and foreign equivalents.

In the event we need to repeat, extend, delay or terminate our clinical trials because these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, our clinical trials may need to be repeated, extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates, and we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates or we or they may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed. To

the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be materially and adversely affected.

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

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities may conclude that a financial relationship between us and/or a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authorities 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 authorities and may ultimately lead to the denial of regulatory approval of one or more of our product candidates.

We rely on third-party manufacturers and suppliers to supply our product candidates. The loss of our third-party manufacturers or suppliers, or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, within acceptable timeframes, or at all, would materially and adversely affect our business.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities for drug manufacturing, storage, distribution or quality testing. We currently rely, and expect to continue to rely, on third parties for the manufacture of active pharmaceutical ingredients ("API"), bulk drug substances, raw materials, samples, components and other materials for our product candidates for clinical testing, as well as for the manufacture of any products candidates that we commercialize, if approved. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, terminated or will be of satisfactory quality or be available at acceptable prices. In addition, if any biotechnology companies or CMOs become subject to trade restrictions, sanctions, or other regulatory requirements by the U.S. government, such actions could restrict or even prohibit our ability to work with such entities. Such disruption could have adverse effects on the development of our product candidates and our business operations. Also, any replacement of our manufacturer could require significant effort and time because there may be a limited number of qualified replacements.

We obtain our preclinical and clinical supplies from our manufacturers on a purchase order basis, and currently do not have long-term supply arrangements in place. The manufacturing process for our product candidates is subject to the FDA and foreign regulatory authority review. We, and our 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 regulatory standards, such as cGMPs. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory authorities, we may not be able to rely on their facilities for the manufacture of elements of our product candidates. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA, and comparable foreign regulatory authorities. If the FDA or any comparable foreign regulatory authority determines that our third-party manufacturers' facilities are not in compliance with applicable laws and regulations, including those governing cGMPs, they may deny any NDA or marketing application we submit until the deficiencies are corrected or we replace the manufacturer in our application with a manufacturer that is able to demonstrate a compliance status acceptable to the FDA or foreign regulatory authority. Moreover, we are dependent on our CMOs for manufacturing in compliance with cGMPs and other regulatory requirements. In the event that any of our manufacturers

fails to comply with such requirements or to perform its obligations in relation to quality, timing or otherwise, or if our projected manufacturing capacity or supply of materials becomes limited, interrupted, or more costly than anticipated, we may be forced to enter into an agreement with another third party, which we may not be able to do timely or on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such to another third party. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture our product candidates. We will be required to verify that the new manufacturer maintains facilities and procedures that comply with applicable quality standards and regulations and guidelines; and we may be required to repeat some of the development program. If we are required to change manufacturers, the delays and costs associated with the verification of a new manufacturer, whether due to failure to comply with regulatory requirements, or quality, timing and supply issues, or other reason, could negatively affect our ability to develop product candidates in a timely manner or within budget.

As part of our process development efforts, we also may make changes to the manufacturing processes at various points during development, for various reasons, such as controlling costs, achieving scale, decreasing processing time, improving product formulations, increasing manufacturing success rate or other reasons. For example, we are implementing certain manufacturing process changes for ESK-001 to increase scalability with respect to our Phase 3 clinical trials. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our current or future product candidates to perform differently and affect the results of our future clinical trials. In some circumstances, changes in the manufacturing process may require us to perform *ex vivo* comparability studies or clinical bridging studies, and we may be required to collect additional data from participants prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial.

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

- an inability to initiate or continue preclinical studies or clinical trials of product candidates;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of future collaborators;
- sanctions being imposed on us, including shutdown of the third-party vendor or invalidation of drug product lots or processes, fines, injunctions, civil penalties, delays, suspension, variation or withdrawal of approvals, license revocation, seizures of product candidates or drugs, operating restrictions and criminal prosecutions;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

Additionally, our CMOs may experience difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our CMOs were to encounter any of these difficulties, our ability to provide our product

candidates to participants in preclinical and clinical trials, or to provide product for treatment of participants once approved, would be jeopardized.

We depend on limited source suppliers for certain raw materials used in our product candidates. If we are unable to source these supplies on a timely basis or establish redundancy in our manufacturing process or longer-term contracts with our CMOs, we will not be able to complete our clinical trials on time and the development of our product candidates may be delayed.

Certain of the raw materials necessary to produce ESK-001 and A-005 are in limited supply, and we generally rely on one CMO for each manufacturing stage. While we intend to identify and qualify additional suppliers and redundant manufacturers to provide the API, drug product and critical raw material prior to submission of an NDA to the FDA and/or a comparable marketing application outside the United States, there can be no assurance that we will be successful in doing so. Furthermore, any of the limited source suppliers upon whom we rely could stop producing our supplies, cease operations or be acquired by, or enter into exclusive arrangements with, our competitors. Establishing redundancy in CMOs and additional or replacement suppliers for these supplies, and obtaining regulatory authorizations that may result from adding or replacing CMOs and suppliers, could take a substantial amount of time, result in increased costs and impair our ability to produce our products, which would adversely impact our business, financial condition, results of operations and prospects. Any such interruption or delay may force us to seek similar supplies from alternative sources, which may not be available at reasonable prices, or at all. Any interruption in the supply of limited source components for our product candidates would adversely affect our ability to meet scheduled timelines and budget for the development and commercialization of our product candidates, could result in higher expenses and would harm our business. Although we have not experienced any significant disruption as a result of our reliance on limited source suppliers, we have a limited operating history and cannot assure you that we will not experience disruptions in our supply chain in the future as a result of such reliance or otherwise.

In addition, we do not currently have long-term supply contracts with our CMOs, and they are not obligated to supply drug products to us for any period, in any specified quantity or at any certain price beyond the delivery contemplated by the relevant purchase orders. As a result, our suppliers could stop selling to us at commercially reasonable prices, or at all. While we intend to enter into long-term master supply agreements with certain of our CMOs prior to any potential NDA submission, we may not be successful in negotiating such agreements on favorable terms or at all. If we do enter into such long-term master supply agreements, or enter into such agreements on less favorable terms than we currently have with such manufacturers, we could be subject to binding long-term purchase obligations that may be harmful to our business, including in the event that we do not conduct our trials on planned timelines, or at all, or utilize the drug products that we are required to purchase. Any change in our relationships with our CMOs or changes to the contractual terms of our agreements with them could adversely affect our business, financial condition, results of operations and prospects.

The operations of our suppliers, most of which are located outside of the United States, are subject to additional risks that are beyond our control and that could harm our business, financial condition, results of operations and prospects.

Currently, most of our suppliers are located outside of the United States. As a result of our global suppliers, we are subject to risks associated with doing business abroad, including:

- political unrest, terrorism, labor disputes, and economic instability resulting in the disruption of trade from foreign countries in which our products are manufactured;
- the imposition of new laws and regulations, including those relating to labor conditions, quality, and safety standards, imports, duties, taxes, and other charges on imports, as well as trade restrictions and restrictions on currency exchange or the transfer of funds, particularly new or increased tariffs imposed on imports from countries where our suppliers operate;
- greater challenges and increased costs with enforcing and periodically auditing or reviewing our suppliers' and manufacturers' compliance with cGMPs or status acceptable to the FDA or comparable foreign regulatory authorities;

- reduced protection for intellectual property rights, including trademark protection, in some countries particularly China;
- disruptions in operations due to global, regional, or local public health crises or other emergencies or natural disasters, including, for example, disruptions experienced during the COVID-19 pandemic;
- disruptions or delays in shipments; and
- changes in local economic conditions in countries where our manufacturers or suppliers are located.

These and other factors beyond our control could interrupt our suppliers' production, influence the ability of our suppliers to export our clinical supplies cost-effectively or at all, and inhibit our suppliers' ability to procure certain materials, any of which could harm our business, financial condition, results of operations and prospects.

Risks Related to Ownership of Our Common Stock

As a result of our history of losses and negative cash flows from operations, our consolidated financial statements contain a statement regarding a substantial doubt about our ability to continue as a going concern.

Our history of operating losses and negative cash flows from operations combined with our anticipated use of cash to fund operations raises substantial doubt about our ability to continue as a going concern as our existing cash, cash equivalents and marketable securities of \$288.3 million as of December 31, 2024 will not be sufficient to meet operating and capital requirements for at least 12 months from the date of issuance of our audited consolidated financial statements included in Part II, Item 8. of this Annual Report on Form 10-K. Based on our current operating plan, we will need to raise additional financing to continue our products' development for the foreseeable future, and until we become profitable. Our future viability as an ongoing business is dependent on our ability to generate cash from our operating activities or to raise additional capital to finance our operations.

If we are unable to raise additional capital as and when needed, our business, financial condition and results of operations will be materially and adversely affected, and we may be forced to delay our development efforts, limit our activities and reduce research and development costs. If we are unable to continue as a going concern, we may have to liquidate our assets, and the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements. The inclusion of a going concern explanatory paragraph by our independent registered public accounting firm, our lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital, enter into licensing and collaboration arrangements or other contractual relationships with third parties and otherwise execute our development strategy.

An active and liquid trading market for our common stock may not develop, and you may not be able to resell your shares of common stock at or above the price you paid for them.

An active trading market for our common stock may never develop or, if it is developed, be sustained. The market value of our common stock may decrease from the price you paid for them. As a result of these and other factors, including our limited public float, you may be unable to resell your shares of our common stock at or above the price you paid for them. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

Our quarterly and annual operating results, and the combined company's results, if the proposed Merger is consummated, may fluctuate significantly or may fall below the expectations of investors or securities analysts or any guidance we may publicly provide, each of which may cause our stock price to fluctuate or decline.

We expect our operating results, and the combined company's results, if the proposed Merger is consummated, to be subject to quarterly and annual fluctuations which may, in turn, cause the price of our common stock to fluctuate substantially. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of our most advanced product candidate ESK-001, A-005 and other development programs;
- results and timing of preclinical studies and ongoing and future clinical trials, or the addition or termination of any such clinical trials;
- the timing of payments we may make or receive under future license and future collaboration arrangements or the termination or modification thereof;
- our execution of any strategic transactions, including the proposed Merger and any future acquisitions, collaborations, licenses or similar arrangements, and the timing and amount of payments we may make or receive in connection with such transactions;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- recruitment and departures of key personnel;
- if our product candidates receive regulatory approval, the terms of such approval and market acceptance and demand for such products;
- regulatory developments affecting our product candidates or those of our competitors;
- fluctuations in stock-based compensation expense;
- the impacts of inflation, rising interest rates and tariffs and escalating trade tensions on our business and operations; and
- changes in general market and economic conditions.

If our quarterly or annual operating results (or the combined company's results, if the proposed Merger is consummated) fall below the expectations of investors or securities analysts or any forecasts or guidance we may provide to the market, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide. We believe that quarterly or annual comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Our stock price is likely to continue to be volatile, which could result in substantial losses for our investors.

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

- volatility and instability in the financial and capital markets;
- announcements relating to our product candidates, including the results of clinical trials by us or any future collaborators;

- announcements by competitors that impact our competitive outlook;
- negative developments with respect to our product candidates, or similar products or product candidates with which we compete;
- developments with respect to patents or intellectual property rights;
- announcements of technological innovations, new product candidates, new products or new contracts by us or our competitors;
- announcements relating to the proposed Merger and any future strategic transactions, including acquisitions, collaborations, licenses or similar arrangements;
- actual or anticipated variations in our operating results due to the level of development expenses and other factors;
- changes in financial estimates by equities research analysts and whether our earnings (or losses) meet or exceed such estimates;
- announcement or expectation of additional financing efforts and receipt, or lack of receipt, of funding in support of conducting our business;
- sales of our common stock by us, our insiders, or other stockholders, or issuances by us of shares of our common stock in connection with strategic transactions such as the proposed Merger;
- conditions and trends in the pharmaceutical, biotechnology and other industries;
- regulatory developments within, and outside of, the United States, including changes in the structure of health care payment systems;
- litigation or arbitration;
- COVID-19 or other pandemics, natural disasters, or major catastrophic events;
- general economic, political and market conditions and other factors; and
- the occurrence of any of the risks described in this section titled “Risk Factors.”

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance.

Sales of a substantial number of shares of our common stock could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly. Immediately following the Merger, our pre-Merger equityholders are expected to hold approximately 55% of the combined company’s common stock and the pre-Merger equityholders of ACELYRIN are expected to hold approximately 45% of the combined company’s common stock, in each case, calculated on a fully diluted basis as of January 31, 2025. Upon consummation of the Merger, shares of our common stock issued in the Merger, will be freely tradeable in the public market.

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

We also expect that significant additional capital may be needed in the future to continue our planned operations, including conducting our planned clinical trials, manufacturing and commercialization efforts, expanded research and development activities and costs associated with operating as a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

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

Based on the beneficial ownership of our capital stock as of December 31, 2024, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 72% of our outstanding voting stock. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise. In addition, as a result of this concentration of ownership, there is a limited number of shares of our common stock that are not held by officers, directors and controlling stockholders (which is referred to as our public float), thereby adversely impacting the liquidity of our common stock and potentially depressing the price at which you may be able to sell shares of common stock.

We are an “emerging growth company” and a “smaller reporting company” and the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an “emerging growth company” as defined in Section 2(a) of the Securities Act of 1933, as amended (the “Securities Act”), as modified by the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to the other public companies that are not “emerging growth companies,” including (i) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, (ii) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (iii) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting obligations in this report. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. These provisions allow an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of such extended transition period. We cannot predict whether investors will find our common stock less attractive as a result of its reliance on these exemptions. If some investors find our common stock to be less attractive as a result, there may be a less active trading market for our common stock and the price of our common stock may be more volatile than the current trading market and price of our common stock.

Further, there is no guarantee that the exemptions available under the JOBS Act will result in significant savings. To the extent that we choose not to use exemptions from various reporting requirements under the JOBS Act, we will incur additional compliance costs, which may impact our financial condition.

We will remain an emerging growth company until the earliest of: (i) the end of the fiscal year in which we have a total annual gross revenue of \$1.235 billion; (ii) the last day of our fiscal year following the fifth anniversary of the completion

of our initial public offering (“IPO”); (iii) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt; or (iv) the end of the fiscal year in which the market value of common stock held by non-affiliates exceeds \$700 million as of the prior June 30. Even after we no longer qualify as an emerging growth company, we may continue to qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation. In addition, if we are a smaller reporting company with less than \$100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act.

Anti-takeover provisions in our charter documents and under Delaware law could prevent or delay an acquisition of us that may be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed “for cause” and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our amended and restated certificate of incorporation and amended and restated bylaws;
- authorize the issuance of “blank check” preferred stock that our board could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law (“DGCL”) may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

The exclusive forum provisions in our organizational documents may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers or employees, or the underwriters of any offering giving rise to such claim, which may discourage lawsuits with respect to such claims.

Our amended and restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware is the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; or any action asserting a claim that

is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, or the underwriters of any offering giving rise to such claims, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our amended and restated 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 harm our business, financial condition, results of operations and prospects.

Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Our amended and restated bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the Federal Forum Provision), including for all causes of action asserted against any defendant named in such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While federal or other state courts may not follow the holding of the Delaware Supreme Court or may determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court, and our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. In addition, neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court, and our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions in our amended and restated certificate of incorporation, including the Federal Forum Provision. These provisions may limit a stockholders' ability to bring a claim, and may result in increased costs for a stockholder to bring such a claim, in a judicial forum of their choosing for disputes with us or our directors, officers, other employees or agents, which may discourage lawsuits against us and our directors, officers, other employees or agents.

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

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

Because we do not anticipate paying any dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared nor paid dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development, operation and expansion of our business and we do not anticipate declaring

or paying any dividends in the foreseeable future. As a result, capital appreciation of our common stock, which may never occur, will be your sole source of gain on your investment for the foreseeable future.

The dual class structure of our common stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The dual class structure of our common stock may limit your ability to influence corporate matters. Holders of our common stock are entitled to one vote per share, while holders of our non-voting common stock are not entitled to any votes. Nonetheless, each share of our non-voting common stock may be converted at any time into one share of our common stock at the option of its holder by providing written notice to us, subject to the ownership and other limitations provided for in our certificate of incorporation. Consequently, if holders of our non-voting common stock exercise their option to make this conversion, this will have the effect of increasing the relative voting power of those prior holders of our non-voting common stock, and correspondingly decreasing the voting power of the holders of our common stock, which may limit your ability to influence corporate matters. Additionally, stockholders who hold, in the aggregate, more than 10% of our common stock and non-voting common stock, but 10% or less of our common stock, and are not otherwise an insider, may not be required to report changes in their ownership due to transactions in our non-voting common stock pursuant to Section 16(a) of the Exchange Act, and may not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

General Risk Factors

Unstable economic and market conditions may have serious adverse consequences on our business, financial condition and stock price.

Global economic and business activities continue to face widespread uncertainties, and global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, rising inflation and monetary supply shifts, rising interest rates, labor shortages, declines in consumer confidence, declines in economic growth, increases in unemployment rates, recession risks and uncertainty about economic and geopolitical stability (for example, related to the ongoing conflicts in Ukraine and Israel and the surrounding areas). The extent of the impact of these conditions on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected timeframe, as well as that of third parties upon whom we rely, will depend on future developments which are uncertain and cannot be predicted. There can be no assurance that further deterioration in economic or market conditions will not occur, or how long these challenges will persist. If the current equity and credit markets further deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

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

The trading market for our common stock is influenced in part by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over the industry or securities analysts, or the content and opinions included in their reports and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, or if analysts cease coverage of us, we could lose visibility in the financial markets, and the trading price for our common stock could be impacted negatively. If any of the analysts who cover us publish inaccurate or unfavorable research or opinions regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline.

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

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Securities Act, the Exchange Act, Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection

Act, the listing requirements of the Nasdaq Global Select 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. Our management and other personnel will continue to need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly, particularly after we are no longer an emerging growth company. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. The increased costs may require us to reduce costs in other areas of our business. Moreover, 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.

Failure to establish and maintain effective internal control over financial reporting could adversely affect our business and if investors lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could be negatively affected.

We are not currently required to comply with the rules of the SEC implementing Section 404(b) of the Sarbanes-Oxley Act which requires including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, we are required to comply with the SEC's rules implementing Sections 302 and 404(a) of the Sarbanes-Oxley Act, which require our management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of internal control over financial reporting. Although we will be required to disclose changes made in our internal control over financial reporting on a quarterly basis, we will not be required to make our first annual assessment of our internal control over financial reporting until our second annual report on Form 10-K. Furthermore, as an emerging growth company, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting until the later of the year following our first annual report required to be filed with the SEC or the date we are no longer an emerging growth company. At such time, our independent registered public accounting firm would need to issue a report that is adverse in the event that there are material weaknesses in our internal control over financial reporting.

To comply with the requirements of being a public company, we have undertaken various actions, and will need to take additional actions, such as implementing numerous internal controls and procedures and hiring additional accounting or internal audit staff or consultants. Testing and maintaining internal controls can divert our management's attention from other matters that are important to the operation of our business. Additionally, when evaluating our internal control over financial reporting, we may identify material weaknesses that we may not be able to remediate in time to meet the applicable deadline imposed upon us for compliance with the requirements of Section 404(b). If we identify any material weaknesses in our internal control over financial reporting or are unable to comply with the requirements of Section 404(b) in a timely manner or assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting once we are no longer an emerging growth company, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could be negatively affected, and we could become subject to investigations by the stock exchange on which our securities are listed, the SEC or other comparable foreign regulatory authorities, which could require additional financial and management resources. In addition, if we fail to remedy any material weakness, our financial statements could be inaccurate, and we could face restricted access to capital markets.

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

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

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. In addition, we do not have a formal risk management program for identifying and addressing risks to our business in other areas.

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

The market price of our common stock is likely to be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation (including the cost to defend against, and any potential adverse outcome resulting from any such proceeding) can be expensive and time-consuming, damage our reputation and divert our management's attention from other business concerns, which could seriously harm our business.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Risk Management and Strategy

We manage cybersecurity risks utilizing a risk-based approach that incorporates various information security processes designed to identify, assess and manage risks from cybersecurity threats, including potential unauthorized access to our critical information technology systems and data. Depending on the environment, we maintain certain controls, systems, and other processes designed to identify, assess and manage our cybersecurity threats and risks, such as: maintaining network security controls, maintaining email security tools, utilizing certain third-party managed security services, such as managed detection and response, monitoring threat intelligence bulletins, conducting penetration tests and vulnerability scans, maintaining cybersecurity insurance, and conducting periodic employee cybersecurity training.

Our assessment and management of material risks from cybersecurity threats are integrated into the Company's overall enterprise risk management processes. For example, we evaluate and manage material risks arising from cybersecurity threats, along with other significant risks we face, against our overall business objectives and within our overall enterprise risk management practices. The audit committee of our board of directors (the "Audit Committee") evaluates our overall enterprise risks.

We use service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example, outside security consultants and vendors, third party penetration testing providers, and forensic providers.

Further, we use third-party service providers to perform a variety of functions throughout our business, such as software-as-a-service providers, data hosting companies, and contract research organizations. We maintain a vendor risk management process designed to help manage cybersecurity risks associated with our use of these providers. Depending on the nature of the services provided, the sensitivity of the Company systems and data at issue, and the identity of the provider, our vendor risk management process may involve different levels of assessment designed to help identify cybersecurity risks associated with a provider, including, for example, security questionnaires and the imposition of contractual obligations related to cybersecurity on the provider.

For a description about risks from cybersecurity threats that may materially affect the Company and how they may do so, see our Risk Factors under Part I, Item 1A., under the heading "*If our information technology systems, or those used by*

our CROs, CMOs, clinical sites or other third parties with whom we work, or our data are or were compromised, become unavailable or suffer security breaches, loss or leakage of data or other disruptions, we could suffer material adverse consequences resulting from such compromise, including but not limited to, operational or service interruption, harm to our reputation, regulatory investigations or actions, litigation, fines, penalties and liability, and other adverse consequences to our business, results of operations, and financial condition.”

Governance

The board of directors addresses the Company’s cybersecurity risk management as part of its general oversight function. The Audit Committee has been designated by our board of directors to oversee the Company’s cybersecurity risk management process, including oversight of mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by a dedicated information technology team, led by our Executive Director of Information Technology who has over twenty years of experience managing information technology systems and cybersecurity risks and who reports directly to our Chief Financial Officer. Our Executive Director of Information Technology is responsible for hiring appropriate personnel, helping to integrate cybersecurity risk considerations into the Company’s overall risk management strategy, and communicating key priorities to relevant personnel. Our Executive Director of Information Technology, together with certain other senior management personnel, is responsible for approving functional cybersecurity budgets, implementing approved, phase-appropriate cybersecurity policies, plans and/or guidelines, reviewing security assessments and other security-related reports and overseeing cybersecurity processes.

Our incident response processes are designed to escalate certain incidents to members of management (including the Chief Financial Officer) depending on the circumstances. Our Executive Director of Information Technology works with the Company’s cybersecurity incident responders to help the Company mitigate and remediate cybersecurity incidents of which they are notified. The Company’s incident response processes also include reporting to the Disclosure Committee and the Audit Committee for certain cybersecurity incidents. In addition, the Audit Committee receives periodic updates on cybersecurity risks and information technology matters, including related risk exposures and the processes the Company has implemented to address them, from management.

Item 2. Properties

Our principal executive office is located in South San Francisco, California. We entered into the lease for our principal executive office in August 2022, for approximately 55,000 square feet of combined office and laboratory space in South San Francisco, which will expire in August 2033. In December 2024, we entered into a lease for approximately 22,000 square feet of additional office space in South San Francisco, California. The lease began in January 2025, and the lease term will end in December 2026. We believe our facilities are adequate and suitable for our current needs, and that should it be needed, suitable additional or alternative space will be available to accommodate our operations.

Item 3. Legal Proceedings

From time to time, we may become involved in material legal proceedings or be subject to claims arising in the ordinary course of our business. We are currently not party to any legal proceedings material to our operations or of which any of our property is the subject, nor are we aware of any such proceedings that are contemplated by a government authority. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources, negative publicity, reputational harm and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Common Stock

Our voting common stock has been listed on The Nasdaq Global Select Market under the symbol “ALMS” since June 28, 2024. Prior to that date, there was no public market for our common stock.

Holders of Common Stock

As of March 12, 2025, there were 67 stockholders of record of our voting common stock and 2 stockholders of our non-voting common stock. Because many of our voting common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividend Policy

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

Unregistered Sales of Equity Securities

Equity Plan-Related Issuances

From January 1, 2024 through June 30, 2024, we granted certain directors, officers, employees, consultants and other service providers options to purchase an aggregate of (i) 1,796,797 shares of our common stock under our 2021 Stock Plan (the “2021 Plan”) at exercise prices ranging from \$8.84 to \$13.32 per share, (ii) 1,880,680 shares of our common stock under our 2024 Performance Option Plan (the “2024 POP”) at an exercise price of \$10.19 per share and (iii) 163,131 shares of our common stock under our 2024 Equity Incentive Plan (the “2024 EIP”) at an exercise price of \$16.00 per share.

Redeemable Convertible Preferred Stock Issuances

In May 2024, we sold an aggregate of 41,264,892 shares of our Series C redeemable convertible preferred stock at a purchase price of \$3.13826 per share. The aggregate purchase price for the Series C redeemable convertible preferred shares was \$129,499,960.

Concurrent Private Placement

In connection with our IPO, we completed a concurrent private placement that closed on July 17, 2024, in which we issued and sold 2,500,000 shares of common stock at \$16.00 per share, the IPO price, to AyurMaya Capital Management Fund, LP, an existing investor (the “Concurrent Private Placement”). This transaction did not involve any underwriters, underwriting discounts or commissions, or any public offering.

The offers, sales and issuances of the securities described in the preceding paragraphs were deemed to be exempt from registration under the Securities Act in reliance on Section 4(a)(2) of the Securities Act or Rule 506 of Regulation D promulgated thereunder as a transaction by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any

distribution thereof. Each of the recipients of securities in these transactions was either an accredited investor within the meaning of Rule 501 of Regulation D under the Securities Act or had adequate access, through employment, business or other relationships, to information about us. Appropriate legends were affixed to the securities issued in these transactions.

Use of Proceeds from our Initial Public Offering of Common Stock and Concurrent Private Placement

On June 27, 2024, our Registration Statement on Form S-1, as amended (File No. 333-280068) (the “Registration Statement”), was declared effective in connection with our IPO, pursuant to which we sold an aggregate of 13,125,000 shares of our common stock at a price to the public of \$16.00 per share. Morgan Stanley & Co. LLC, Leerink Partners LLC, Cantor Fitzgerald & Co. and Guggenheim Securities, LLC acted as joint book-running managers. The IPO closed on July 1, 2024. The aggregate net proceeds from the IPO were \$193.3 million, after deducting underwriting discounts and commissions and other offering costs of \$16.7 million. The offering terminated after the sale of all securities registered pursuant to the Registration Statement. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

In connection with the IPO, we completed the Concurrent Private Placement that closed on July 17, 2024, in which we issued and sold 2,500,000 shares of common stock at \$16.00 per share, the IPO price, to AyurMaya Capital Management Fund, LP, an existing investor.

The net proceeds from our IPO and Concurrent Private Placement have been invested according to our approved investment policy in a mix of money market funds and high-quality, available-for-sale marketable securities. There has been no material change in the planned use of proceeds from our IPO as described in the Company’s final prospectus for its IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 28, 2024.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. This discussion and analysis and other parts of this Annual Report on Form 10-K contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives and expectations for our business. Our actual results and the timing of selected events could differ materially from those described or implied by these forward-looking statements as a result of several factors, including those set forth under Part I, Item 1A. “Risk Factors” in this Annual Report on Form 10-K. See also see the section titled “Special Note Regarding Forward-Looking Statements.”

Overview

Our mission is to significantly improve the lives of patients by replacing broad immunosuppression with targeted therapies. Our name, Alumis, captures our mission to enlighten immunology, and is inspired by the words “allumer”—French for illuminate—and “immunis”—Latin for the immune system.

We are a clinical stage biopharmaceutical company with an initial focus on developing our two TYK2 inhibitors: ESK-001, a second-generation inhibitor that we are developing to maximize target inhibition and optimize tolerability, and A-005, a CNS penetrant molecule. ESK-001 has demonstrated significant therapeutic effect in our Phase 2 program in patients with PsO, and is currently being evaluated in an additional Phase 2 clinical trial in patients with SLE, for which we expect to report results in 2026. With the favorable results in our Phase 2 clinical trial in PsO, we have initiated our Phase 3 ONWARD clinical program, which consists of two parallel Phase 3 clinical trials of ESK-001 in this indication and for which we expect to report topline results in the first quarter of 2026. These parallel Phase 3 clinical trials also include one LTE study, ONWARD3. In addition, the OLE of our Phase 2 clinical trial in PsO remains ongoing. TYK2 genetic mutations are associated with a strong protective effect in MS, motivating us to develop our second product candidate, A-005, as a CNS-penetrant, allosteric TYK2 inhibitor for neuroinflammatory and neurodegenerative diseases. In April 2024, we initiated our Phase 1 program of A-005 in healthy volunteers and reported initial results in December 2024.

Alumis was incubated by Foresite Labs and incorporated on January 29, 2021, as a Delaware corporation under the name FL2021-001, Inc. FL2021-001, Inc.’s name was changed to Esker Therapeutics, Inc. in March 2021, and to Alumis Inc. in January 2022.

Since our inception, we have devoted substantially all of our efforts to organizing our company, hiring personnel, business planning, acquiring and developing our product candidates, performing research and development, conducting preclinical studies and clinical trials, establishing and protecting our intellectual property portfolio, raising capital and providing general and administrative support for these activities. We do not have any products approved for sale and have not generated any revenue from product sales. We expect to continue to incur significant and increasing expenses and increasing substantial losses for the foreseeable future as we continue our development of and seek regulatory approvals for our product candidates and commercialize any approved products, seek to expand our product pipeline and invest in our organization. Our ability to achieve and sustain profitability will depend on our ability to successfully develop, obtain regulatory approval for and commercialize our product candidates. There can be no assurance that we will ever earn revenue or achieve profitability, or if achieved, that the revenue or profitability will be sustained on a continuing basis.

To date, we have primarily funded our operations with proceeds from sales of shares of our common stock and redeemable convertible preferred stock and the issuance of convertible promissory notes in private placements. In July 2024, we closed our IPO and the Concurrent Private Placement and received \$233.3 million in net proceeds, after deducting underwriting discounts and commissions and offering expenses payable by the Company. As of December 31, 2024, we had \$288.3 million in cash, cash equivalents and marketable securities.

We have incurred significant operating losses and negative cash flows since our inception. Our net loss for the years ended December 31, 2024 and 2023 was \$294.2 million and \$155.0 million, respectively. As of December 31, 2024, we had an accumulated deficit of \$658.6 million. Substantially all of our net losses have resulted from costs incurred in connection

with our research and development efforts, including acquisitions of in-process research and development assets, and, to a lesser extent, from general and administrative costs associated with our operations. Our net losses and operating losses may fluctuate from quarter to quarter and year to year depending primarily on the timing of acquisition of any new product candidates, the timing of our preclinical studies and clinical trials, our other research and development expenses, and the timing and amount of any milestone or royalty payments due under our existing or future license agreements. In addition, we have incurred and will continue to incur additional costs associated with operating as a public company, including significant legal, audit, accounting, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer liability insurance costs, investor and public relations costs, and other expenses that we did not incur as a private company.

We anticipate that our expenses will increase significantly in connection with our ongoing activities, particularly if and as we:

- continue to progress the development of our product candidates in multiple clinical trials in parallel;
- continue committing substantial capital resources to the contemplated Merger, and if the Merger closes, the anticipated integration and development activities related to the acquired ACELYRIN business;
- explore additional indications for our existing product candidates;
- hire additional clinical, scientific and operational personnel;
- obtain, maintain, expand and protect our intellectual property rights;
- make royalty, milestone, or other payments under the FronThera Acquisition agreement and any future license or collaboration agreements;
- seek to identify, acquire or in-license new technologies or product candidates;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- procure manufacturing and supply chain capacity for our product candidates, including commercial manufacturing readiness and scale-up;
- experience any delays, challenges or other issues associated with the clinical development and regulatory approvals of our product candidates;
- add operational, legal, financial and management information systems and personnel to support our product development, clinical execution and planned future commercialization efforts, as well as to support our transition to a public company;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval; and
- operate as a public company.

We do not have any products approved for sale and have not generated any revenue from product sales since our inception. We do not expect to generate revenue from any product candidates that we develop until we obtain regulatory approval for one or more of such product candidates and commercialize our products or enter into collaboration agreements with third parties. Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we may never achieve or sustain profitability and, unless and until we are able to develop and commercialize our product candidates, we will need to continue to raise additional capital. Until such time as we can generate significant revenue

from product sales, if ever, we expect to finance our operations through public or private equity or debt financings, or potentially other capital sources, such as collaboration or licensing arrangements with third parties or other strategic transactions. There are no assurances that we will be successful in obtaining an adequate level of financing to support our business plans when needed on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration or licensing arrangements with third parties or other strategic transactions, we may have to relinquish rights to our intellectual property, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise capital as and when needed, or on attractive terms, we may have to significantly delay, reduce, or discontinue the development and commercialization of our product candidates or scale back or terminate our pursuit of new in-licenses and acquisitions.

We do not currently own or operate any manufacturing facility. We rely on CMOs to produce our product candidates in accordance with the FDA current cGMP regulations for use in our clinical studies. We have entered into development and manufacturing agreements with various CMOs relating to process development, manufacturing of drug substance and drug product, and quality testing of our product candidates. We expect to rely on our CMOs in the future for the manufacturing of our product candidates in order to expedite readiness for future clinical trials. Most of these CMOs have demonstrated capability in preparation of materials for commercialization. Additionally, we may decide to build our own manufacturing facility in the future to provide us greater flexibility and control over our clinical or commercial manufacturing needs.

Given our stage of development, we do not yet have a marketing or sales organization or commercial infrastructure; however, we intend to build the necessary sales, marketing and commercialization capabilities and infrastructure over time as our product candidates advance through clinical development. We expect to spend a significant amount in commercial development and marketing costs prior to obtaining regulatory and marketing approval of one or more of our product candidates.

IPO and Concurrent Private Placement

On June 27, 2024, our Registration Statement on Form S-1 for our IPO was declared effective, and, on July 1, 2024, we completed our IPO, pursuant to which we issued and sold 13,125,000 shares of our common stock at \$16.00 price per share to the public. Net proceeds from the IPO were \$193.3 million, after deducting underwriting discounts and commissions and other offering costs totaling \$16.7 million.

In connection with the IPO, an existing investor and a holder of more than 5% of our capital stock, purchased an additional 2,500,000 shares of our common stock at the IPO price per share for total gross and net proceeds of \$40.0 million in the Concurrent Private Placement. The closing of the Concurrent Private Placement was contingent on the closing of the IPO. The sale of such shares is not registered under the Securities Act, and as such, the shares may not be offered or sold absent registration or an applicable exemption from registration. The shares sold in connection with the Concurrent Private Placement are subject to existing resale registration rights and were subject to a 180-day lock-up agreement with the underwriters in the IPO. The Concurrent Private Placement closed on July 17, 2024.

Immediately prior to the closing of the IPO on July 1, 2024, all of the shares of our redeemable convertible preferred stock then outstanding converted into 28,855,656 shares of Class A common stock and 7,184,908 shares of Class B common stock at a 1-for-4.675 conversion ratio. All outstanding Class A common stock shares and all outstanding Class B common stock shares were redesignated immediately thereafter into the same number of shares of common stock and non-voting common stock, respectively.

Macroeconomic Trends

Our business and results of operations may be affected by worldwide economic conditions, which may continue to be impacted by global macroeconomic challenges and uncertainty in the markets, including severely diminished liquidity and credit availability, rising inflation and monetary supply shifts, rising interest rates, labor shortages, declines in consumer

confidence, declines in economic growth, increases in unemployment rates, recession risks and uncertainty about economic and geopolitical stability (for example, related to the ongoing conflicts in Ukraine and Israel and the surrounding areas). Further, the United States and other countries have imposed and may continue to impose new trade restrictions and export regulations, have levied tariffs and taxes on certain goods, and could significantly increase tariffs on a broad array of goods. For example, the current Trump administration has proposed or enacted tariffs and substantial changes to trade policies, which could adversely affect our business, including imposing tariffs on certain foreign products, most recently from China, that have and may result in retaliatory tariffs on U.S. goods and services. The effect of macroeconomic conditions may not be fully reflected in our results of operations until future periods. Moreover, negative macroeconomic conditions could adversely impact our ability to obtain financing in the future on terms acceptable to us, or at all. To date, the macroeconomic trends discussed above have not had a material adverse impact on our business, financial condition or results of operations. If, however, economic uncertainty increases or the global economy worsens, our business, financial condition and results of operations may be harmed.

Recent Development

On February 6, 2025, we entered into the Merger Agreement, with ACELYRIN and Merger Sub. Under the terms of the Merger Agreement, Merger Sub will merge with and into ACELYRIN, with ACELYRIN continuing as a direct wholly owned subsidiary of ours. The Merger Agreement was approved by the disinterested directors on our board and the board of directors of ACELYRIN and is subject to stockholder approval by the stockholders of each company and the satisfaction or waiver of other closing conditions.

In connection with the Merger, all of the issued and outstanding shares of common stock of ACELYRIN will be cancelled and converted into the right to receive 0.4274 shares of our common stock, without interest and, if applicable, cash in lieu of fractional shares, subject to any applicable withholding. ACELYRIN's outstanding and unexercised stock options with exercise prices of \$18.00 or less, outstanding and unvested RSUs and performance RSUs will be converted into options to purchase shares of our common stock and restricted stock awards based on the Exchange Ratio. Stock options' exercise price will be adjusted based on the Exchange Ratio as well. ACELYRIN's outstanding and unexercised stock options with exercise prices more than \$18.00 will be cancelled. The Merger Agreement contains certain termination rights for both ACELYRIN and us, including the right of either party to terminate the Merger Agreement if the transactions have not been consummated prior to July 7, 2025. ACELYRIN or we will pay a termination fee of \$10.0 million or \$10.0 million, respectively, under certain circumstances, including termination to accept and enter into a definitive agreement with respect to a superior proposal.

Immediately following the Merger, our pre-Merger equityholders are expected to collectively own approximately 55% of the shares of the combined company and the pre-Merger equityholders of ACELYRIN as of immediately prior to the Merger are expected to collectively own approximately 45% of the combined company, in each case, calculated on a fully diluted basis as of January 31, 2025.

For additional information on the Merger and Merger Agreement, see Note 15 to our consolidated financial statements, in Part II, Item 8. of this Annual Report on Form 10-K.

Components of Results of Operations

Operating Expenses

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

Research and Development Expenses

Research and development expenses consist of external and internal costs primarily related to acquiring and developing our research pipeline and technologies and clinical development of our product candidates.

External costs include:

- costs associated with acquiring technology and intellectual property licenses that have no alternative future uses and costs incurred under in-license or assignment agreements, including milestone payments;
- expenses incurred in connection with the discovery and preclinical development of our pipeline programs;
- costs incurred in connection with the clinical development of our product candidates, including under agreements with CROs, CMOs and other third parties that conduct clinical trials and manufacture clinical supplies, product candidates and components on our behalf; and
- costs for third-party professional research and development consulting services.

Internal costs include:

- research and development personnel-related costs, including salaries, annual bonuses, benefits, travel and meals expenses and stock-based compensation expense; and
- allocated facilities and other overhead costs, including software licenses, computer supplies and accessories and other miscellaneous expenses.

We have acquired and may continue to acquire the rights to develop and commercialize new product candidates. Upfront and milestone payments are accrued for and expensed as in process research and development (“IPR&D”) assets expense when the achievement of the milestone is probable up to the point of regulatory approval and, absent obtaining such approval, have no alternative future use. Milestone payments made after a product’s regulatory approval will be capitalized and amortized over the remaining useful life of the related product.

We expense research and development costs as incurred. Costs of certain activities are recognized based on an evaluation of the progress to completion of specific tasks. However, payments made prior to the receipt of goods or services that will be used or rendered for future research and development activities are deferred and capitalized as research and development prepaid expenses in our consolidated balance sheets. The capitalized amounts are recognized as expense as the goods are delivered or services are performed. Since our inception and through December 31, 2024, our external research and development expenses were primarily related to the discovery and advancement of programs under our TYK2 platform, including our two most advanced product candidates, ESK-001 and A-005. We use internal resources primarily for managing our research, process development, manufacturing and clinical development activities. In particular, with respect to internal costs, we deploy our personnel across all of our research and development activities as our employees work across multiple programs, and therefore the costs cannot be allocated to a particular product candidate or research program.

We expect our research and development expenses to increase substantially for the foreseeable future as we advance our product candidates into and through clinical trials, pursue regulatory approval of our product candidates, build our operational and commercial capabilities for marketing our products, if approved, and expand our pipeline of product candidates. The process of conducting the necessary clinical research to obtain regulatory approval is time-consuming, expensive and uncertain. The actual probability of success for our product candidates may be affected by a variety of factors, including the safety and efficacy of our product candidates, clinical data, investment in our clinical programs, competition, manufacturability and commercial viability. It is possible that we may never receive regulatory approval for any of our product candidates. As a result of the uncertainties discussed above, we are unable to determine the duration and completion of costs of our research and development projects or if, when and to what extent we will generate revenue from the commercialization and sale of our product candidates, if approved by the FDA and other comparable foreign regulatory authorities.

Our future research and development costs may vary significantly based on factors such as:

- the timing and progress of our preclinical and clinical development activities;

- the number and scope of preclinical and clinical programs we decide to pursue;
- the costs and timing of manufacturing of our product candidates
- the amount and timing of any milestone payment due under our existing asset acquisition agreement and any future license or collaboration agreements;
- the number of patients that participate in our clinical trials, and per participant clinical trial costs;
- the number and duration of clinical trials required for approval of our product candidates;
- the number of sites included in our clinical trials, and the locations of those sites;
- delays or difficulties in adding trial sites and enrolling participants;
- patient drop-out or discontinuation rates;
- additional safety monitoring if requested by regulatory authorities;
- the phase of development of our product candidates;
- the timing, receipt and terms of any approvals from applicable regulatory authorities including the FDA and comparable foreign regulatory authorities;
- maintaining a continued acceptable safety profile of our product candidates following approval, if any, of our product candidates;
- changes in the competitive outlook;
- the extent to which we establish additional strategic collaborations or other arrangements; and
- the impact of any business interruptions to our operations or to those of the third parties with whom we work.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We anticipate that our total research and development expenses in 2025 will increase compared to 2024 due primarily to higher costs for the development of our product candidates and ACELYRIN research and development activities, if the Merger closes.

General and Administrative Expenses

Our general and administrative expenses consist primarily of personnel-related costs, legal and consulting services, including those relating to intellectual property and corporate matters, marketing expenses and allocated facilities and other overhead costs, including software licenses, computer supplies, insurance and other miscellaneous expenses. Personnel-related costs include salaries, annual bonuses, benefits, travel and meal expenses and stock-based compensation expense for our general and administrative personnel.

We expect that our general and administrative expenses will increase substantially in the future as a result of expanding our operations, including hiring personnel, preparing for potential commercialization of our product candidates and facility occupancy costs, and support of general operations and ACELYRIN general and administrative activities, if the Merger closes. We also expect an increase in costs associated with being a public company, including costs related to accounting, audit, legal, consulting fees, regulatory and tax-related services associated with maintaining compliance with applicable Nasdaq and SEC requirements, additional director and officer insurance costs, and investor and public relations costs.

Other Income (Expense)

Other income (expense) consists primarily of interest income, including amortization of premiums and accretion of discounts on marketable securities and change in fair value of derivative liability.

In May 2023 and in March 2024, in connection with our redeemable convertible preferred stock financings, we issued options to purchase additional shares of redeemable convertible preferred stock at a specified price, which were accounted for as derivative liabilities. Changes in fair value of these derivative liabilities were included in the other income (loss) in the consolidated statement of operations and comprehensive loss for each reporting period until the derivatives were exercised or expired.

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 (dollars in thousands):

| | Year Ended December 31, | | Change | |
|--|-------------------------|---------------------|---------------------|-------|
| | 2024 | 2023 | \$ | % |
| Operating expenses: | | | | |
| Research and development expenses | \$ 265,554 | \$ 137,676 | \$ 127,878 | 93 % |
| General and administrative expenses | 35,200 | 20,498 | 14,702 | 72 % |
| Total operating expenses | 300,754 | 158,174 | 142,580 | 90 % |
| Loss from operations | (300,754) | (158,174) | (142,580) | 90 % |
| Other income (expense): | | | | |
| Interest income | 12,020 | 3,368 | 8,652 | 257 % |
| Change in fair value of derivative liability | (5,406) | (119) | (5,287) | * |
| Other income (expense), net | (93) | (68) | (25) | 37 % |
| Total other income (expense), net | 6,521 | 3,181 | 3,340 | 105 % |
| Net loss | <u>\$ (294,233)</u> | <u>\$ (154,993)</u> | <u>\$ (139,240)</u> | 90 % |

* not meaningful

Research and Development Expenses

The following table summarizes our external and internal research and development expenses for the years ended December 31, 2024 and 2023 (dollars in thousands):

| | Year Ended December 31, | | Change | |
|--|-------------------------|-------------------|-------------------|-------|
| | 2024 | 2023 | \$ | % |
| External costs: | | | | |
| Milestones related to previously acquired IPR&D assets | \$ 23,000 | \$ — | \$ 23,000 | * |
| CRO, CMO and clinical trials | 151,422 | 68,967 | 82,455 | 120 % |
| Professional consulting services | 19,154 | 13,155 | 5,999 | 46 % |
| Other research and development costs | 10,258 | 11,463 | (1,205) | (11)% |
| Internal costs: | | | | |
| Personnel-related costs | 46,774 | 32,068 | 14,706 | 46 % |
| Facilities and overhead costs | 14,946 | 12,023 | 2,923 | 24 % |
| Total research and development expense | <u>\$ 265,554</u> | <u>\$ 137,676</u> | <u>\$ 127,878</u> | 93 % |

* not meaningful

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Research and development expenses increased by \$127.9 million, to \$265.6 million for the year ended December 31, 2024, from \$137.7 million for year ended December 31, 2023.

Milestones related to previously acquired IPR&D assets for the year ended December 31, 2024, included a \$23.0 million clinical milestone payment made in connection with the FronThera Acquisition. No clinical milestones were achieved or probable during the year ended December 31, 2023.

CRO, CMO and clinical trials expenses increased by \$82.5 million, to \$151.4 million for the year ended December 31, 2024, from \$69.0 million for the year ended December 31, 2023, primarily due to an increase in clinical trial and CRO expenses due to increased activities related to our clinical trials for ESK-001 and A-005 and an increase in CMO expenses associated with manufacturing of clinical supplies to support our trials.

Professional consulting services expenses increased by \$6.0 million, to \$19.2 million for the year ended December 31, 2024, from \$13.2 million for the year ended December 31, 2023, primarily due to increased support for our clinical trials for ESK-001, A-005 and other research programs.

Other research and development costs decreased by \$1.2 million, to \$10.3 million for the year ended December 31, 2024, from \$11.5 million for the year ended December 31, 2023, primarily due to timing of preclinical studies to support our clinical trials for ESK-001 and A-005.

Personnel-related costs increased by \$14.7 million, to \$46.8 million for the year ended December 31, 2024, from \$32.1 million for the year ended December 31, 2023, primarily due to increased research and development headcount and included an increase in stock-based compensation expense of \$5.4 million as a result of additional stock options granted, which included awards granted under the 2024 POP.

Facilities and overhead costs increased by \$2.9 million, to \$14.9 million for the year ended December 31, 2024, from \$12.0 million for the year ended December 31, 2023, primarily due to an increase in software license costs and depreciation expenses allocated to research and development activities.

External Costs by Program

During the years ended December 31, 2024 and 2023, our external research and development expenses were primarily related to the clinical development of our ESK-001 program and, to a lesser extent, advancing our A-005 product candidate and research pipeline. The following table summarizes our external costs by program for the years ended December 31, 2024 and 2023 (in thousands):

| | Year Ended December 31, | |
|--|-------------------------|------------------|
| | 2024 | 2023 |
| ESK-001 | \$ 149,941 | \$ 70,414 |
| A-005 | 19,035 | 7,161 |
| Other programs and research and development activities | 34,858 | 16,010 |
| Total external research and development expense | <u>\$ 203,834</u> | <u>\$ 93,585</u> |

General and Administrative Expenses

General and administrative expenses increased by \$14.7 million, to \$35.2 million for the year ended December 31, 2024, from \$20.5 million for the year ended December 31, 2023.

Personnel-related expenses increased by \$9.0 million, to \$20.0 million for the year ended December 31, 2024, from \$11.0 million for the year ended December 31, 2023, primarily due to increased general and administrative headcount and included an increase in stock-based compensation expense of \$5.5 million as a result of additional stock options granted, which included awards granted under the 2024 POP.

Professional consulting services expenses increased by \$5.4 million, to \$13.3 million for the year ended December 31, 2024, from \$7.9 million for the year ended December 31, 2023, primarily due to an increase in consulting services to support our growth, public company requirements, business development and market analysis, and an increase in recruiting costs.

Other Income (Expense), Net

Other income (expense), net increased by \$3.3 million, to \$6.5 million for the year ended December 31, 2024, from \$3.2 million for the year ended December 31, 2023.

Interest income increased by \$8.7 million, to \$12.0 million for the year ended December 31, 2024, from \$3.4 million for the year ended December 31, 2023, primarily as a result of higher balances of cash equivalents and marketable securities.

We recognized a change in fair value of a derivative liability loss of \$5.4 million for the year ended December 31, 2024, related to the derivative liability recognized in connection with our Series C redeemable convertible preferred stock financing entered into in March 2024. The derivative liability was re-measured at fair value and settled in May 2024, when we closed the second tranche of the Series C financing.

We recognized a change in fair value of a derivative liability loss of \$0.1 million for the year ended December 31, 2023, related to the derivative liability recognized in connection with our Series B-2 redeemable convertible preferred stock financing entered into in May 2023. The derivative liability was re-measured at fair value and settled in October 2023, when we closed the second tranche of the Series B-2 financing. See Note 3 to our consolidated financial statements in Part II, Item 8. of this Annual Report on Form 10-K for additional information.

Liquidity, Capital Resources and Capital Requirements

Sources of Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. To date, we have primarily funded our operations with proceeds from sales of shares of our common stock and redeemable convertible preferred stock and the issuance of convertible promissory notes in private placements and, more recently, from our IPO and Concurrent Private Placement. In July 2024, we closed our IPO and the Concurrent Private Placement and received net proceeds of \$193.3 million and \$40.0 million, respectively. See “—Recent Development” above for a discussion of the proposed Merger.

Based on our current operating plan, our existing cash, cash equivalents and marketable securities of \$288.3 million as of December 31, 2024, will not be sufficient to meet our operating and capital requirements for at least 12 months from the date of issuance of our consolidated financial statements included in Part II, Item 8. of this Annual Report on Form 10-K and there is substantial doubt about our ability to continue as a going concern. We expect to continue to incur substantial losses for the foreseeable future, and our transition to profitability will depend upon successful development, approval and commercialization of our product candidates and upon achievement of sufficient revenues to support our cost structure. We do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates. We may never achieve profitability, and unless we do and until then, we will need to continue to raise additional capital. We will need to raise significant additional capital to fund ongoing research and development activities and maintain future operations. We plan to monitor expenses and may raise additional capital through a combination of public and private equity, debt financings, strategic alliances, and licensing arrangements. Our ability to access capital when needed is not assured and, if capital is not available to us when, and in the amounts, needed, on the terms which are favorable, we could be required to delay, scale back, or abandon some or all of our planned development programs and other operations, which could materially harm our business, financial condition and results of operations.

Future Funding Requirements

Our primary uses of cash are to fund our operations, which consist primarily of research and development expenditures related to our programs and, to a lesser extent, general and administrative expenditures. We anticipate that we will continue to incur significant and increasing expenses for the foreseeable future as we continue to advance our product candidates, expand our corporate infrastructure, including the costs associated with being a public company, further our research and development initiatives for our product candidates, and incur costs associated with potential commercialization. In addition, we anticipate committing substantial capital resources to the transactions contemplated by the Merger Agreement and, assuming the consummation of those transactions, the anticipated integration and development activities related to the acquired ACELYRIN business. We are subject to all of the risks typically related to the development of new drug candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We anticipate that we will need substantial additional funding in connection with our continuing operations.

We do not have any products approved for sale and have not generated any revenue from product sales since our inception. We do not expect to generate revenue from any product candidates that we develop until we obtain regulatory approval for one or more of such product candidates and commercialize our products or enter into collaboration agreements with third parties. Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we may never achieve or sustain profitability and, unless and until we are able to develop and commercialize our product candidates, we will need to continue to raise additional capital. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through public or private equity or debt financings, or potentially other capital sources, such as collaboration or licensing arrangements with third parties or other strategic transactions. There are no assurances that we will be successful in obtaining an adequate level of financing to support our business plans when needed on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration or licensing arrangements with third parties or other strategic transactions, we may have to relinquish rights to our intellectual property, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise capital as and when needed, or on attractive terms, we may have to significantly delay, reduce, or discontinue the development and commercialization of our product candidates or scale back or terminate our pursuit of new in-licenses and acquisitions.

Because of the numerous risks and uncertainties associated with research, development and commercialization of our products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including the following:

- the timing, scope, progress and results of our preclinical studies and clinical trials for our current and future product candidates;
- the number, scope and duration of clinical trials required for regulatory approval of our current and future product candidates;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities for our product candidates;
- the cost of manufacturing clinical and commercial supplies as well as scale up of our current and future product candidates;
- the increase in the number of our employees and expansion of our physical facilities to support growth initiatives;
- our ability to establish new, strategic collaborations, licensing or other arrangements;

- the cost of filing and prosecuting our patent applications, and maintaining and enforcing our patents and other intellectual property rights;
- the extent to which we acquire or in-license other product candidates and technologies;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against our product candidates;
- the timing of when we pay our operating expenses;
- the effect of competing technological and market developments;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- our implementation of various computerized informational systems and efforts to enhance operational systems;
- the costs associated with being a public company; and
- other factors, including economic uncertainty and geopolitical tensions, which may exacerbate the magnitude of the factors discussed above.

Cash Flows

The following table summarizes 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 | \$ (255,078) | \$ (129,975) |
| Net cash (used in) provided by investing activities | (113,790) | 60,472 |
| Net cash provided by financing activities | 492,367 | 89,682 |
| Net increase in cash, cash equivalents and restricted cash | <u>\$ 123,499</u> | <u>\$ 20,179</u> |

Operating Activities

Net cash used in operating activities was \$255.1 million and \$130.0 million for the years ended December 31, 2024 and 2023, respectively.

Net cash used in operating activities for the year ended December 31, 2024, was due to our net loss for the period of \$294.2 million, partially offset by changes in non-cash items totaling \$24.4 million and changes in operating assets and liabilities of \$14.8 million. Non-cash items included \$19.5 million related to stock-based compensation expense, \$5.4 million related to the change in fair value of the derivative liability and \$3.2 million related to depreciation and amortization, partially offset by net accretion of discounts on marketable securities of \$3.7 million. The changes in operating assets and liabilities primarily included an increase of \$18.2 million in research and development accrued expenses, an increase of \$8.5 million in accounts payable and a \$3.5 million increase in other accrued expenses and current liabilities, partially offset by an increase of \$10.8 million in research and development prepaid expenses, an increase of \$2.9 million in other prepaid expenses and other assets and a decrease of \$1.9 million in operating lease liabilities.

Net cash used in operating activities for the year ended December 31, 2023, was due to our net loss for the period of \$155.0 million, partially offset by changes in non-cash items of \$13.0 million and changes in operating assets and liabilities of

\$12.0 million. Non-cash items primarily included \$8.6 million of stock-based compensation expense, \$2.0 million of non-cash lease expense and \$1.3 million of depreciation and amortization. The changes in operating assets and liabilities primarily included a decrease of \$5.5 million in research and development prepaid expenses, an increase of \$5.2 million in research and development accrued expenses and an increase of \$2.5 million in other accrued expenses and current liabilities.

Investing Activities

Net cash used in investing activities of \$113.8 million for the year ended December 31, 2024, was related to purchases of marketable securities of \$240.1 million and purchases of property and equipment of \$1.7 million, partially offset by proceeds from maturities of marketable securities of \$128.0 million.

Net cash provided by investing activities of \$60.5 million for the year ended December 31, 2023, was related to proceeds from maturities of marketable securities of \$76.3 million, partially offset by purchases of marketable securities of \$11.3 million and purchases of property and equipment of \$4.5 million.

Financing Activities

Net cash provided by financing activities of \$492.4 million for the year ended December 31, 2024, included net proceeds of \$258.5 million from the issuance of our Series C redeemable convertible preferred stock and related derivative liability, net of offering costs, \$193.3 million net proceeds from our IPO, net of underwriter discounts and commissions and other offering costs, gross and net proceeds of \$40.0 million from a private placement transaction and proceeds of \$0.6 million from the issuance of common stock upon exercise of stock options.

Net cash provided by financing activities of \$89.7 million for the year ended December 31, 2023, was primarily related to net proceeds from the issuance of our Series B-2 and Series B-2A redeemable convertible preferred stock financing.

Contractual Obligations and Commitments

We enter into contracts in the normal course of business with suppliers, CROs, CMOs and clinical trial sites. These agreements provide for termination at the request of either party generally with less than one-year notice and are therefore cancellable contracts. We do not currently expect any of these agreements to be terminated and did not have any non-cancelable obligations under these agreements as of December 31, 2024.

On March 5, 2021, we entered into a stock purchase agreement to acquire FronThera U.S. Holdings, Inc. and its wholly owned subsidiary, FronThera U.S. Pharmaceuticals LLC. The transaction was accounted for as an asset acquisition. Under the agreement, we are obligated to pay contingent consideration of up to an aggregate of \$120.0 million based on the achievement of specified clinical and approval milestones, for up to an aggregate of \$70.0 million payable for clinical milestones, and for up to an aggregate of \$50.0 million payable for approval milestones, all related to technology acquired under the agreement. In the year ended December 31, 2022, we incurred and made a \$37.0 million milestone payment for the first administration of ESK-001 to a patient enrolled in a Phase 2 clinical trial of ESK-001, which was recorded in research and development expenses in the consolidated statements of operations and comprehensive loss. In July 2024, we met a milestone in connection with the first administration of ESK-001 to a patient enrolled in a Phase 3 clinical trial of ESK-001 and made a \$23.0 million milestone payment in August 2024, which was recorded in research and development expenses in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2024. No other milestones were achieved or were probable of being achieved as of December 31, 2024.

We have operating lease arrangements for office and laboratory space in South San Francisco, California. As of December 31, 2024, we had total undiscounted lease payment obligations under non-cancelable leases of \$5.0 million payable in the 12 months following December 31, 2024 and \$43.4 million payable thereafter.

In December 2024, we entered into a lease agreement for approximately 22,000 square feet of additional office space in South San Francisco, California. Total undiscounted lease payments over the lease term beginning in January 2025 will be approximately \$1.9 million.

See Note 7 to our consolidated financial statements in Part II, Item 8. of this Annual Report on Form 10-K for additional information.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our consolidated financial statements in Part II, Item 8. of this Annual Report on Form 10-K for additional information.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported expenses during the reporting period. On an ongoing basis, we evaluate our estimates and assumptions, including but not limited to those related to research and development expenses and accruals, stock-based compensation expense, the fair value of our common stock and the fair value of our derivative liability prior to our IPO. These estimates and assumptions are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates and assumptions could occur in the future. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

Although our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements in Part II, Item 8. of this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Research and Development Expenses and Accruals

Research and development costs are expensed as incurred. As part of the process of preparing our financial statements, we are required to estimate our research and development accrued expenses, including those related to clinical trials and manufacturing clinical and preclinical materials. This process involves reviewing open contracts and purchase orders and communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of actual costs. Our service providers invoice us in arrears, as well as on a pre-determined schedule or when contractual milestones are met. We make estimates of our research and development accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments if necessary. Examples of estimated research and development accrued expenses include fees paid to:

- vendors in connection with preclinical and clinical development activities;
- CROs in connection with clinical trials; and
- CMOs in connection with the process development and scale-up activities and the production of preclinical and clinical trial materials.

Costs for clinical trials and manufacturing activities are recognized based on an evaluation of our vendors' progress towards completion of specific tasks, using data such as participant enrollment, clinical site activations or information provided to us by our vendors regarding their actual costs incurred. Payments for these activities are based on the terms of individual contracts and payment timing may differ significantly from the period in which the services were performed. We determine accrual estimates through reports from and discussions with applicable personnel and outside service

providers as to the progress or state of completion of studies, or the services completed. Our estimates of research and development accrued expenses as of each balance sheet date are based on the facts and circumstances known at the time. Costs that are paid in advance of performance are deferred as a prepaid expense and amortized over the service period as the services are provided.

Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of research and development accrued expenses. However, due to the nature of estimates, we cannot assure that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Stock-Based Compensation Expense

We grant stock-based awards to employees, directors and non-employee consultants in the form of stock options to purchase shares of our common stock. Compensation expense for stock options with service-based vesting conditions is measured at the fair value of the award on the grant date and is recognized over the requisite service period, which is generally the vesting period, using the straight-line method. We estimate the fair value of each stock option with service-based vesting on the date of grant using the Black-Scholes option pricing model. This model requires the use of subjective assumptions to determine the fair value of each stock-based award, including:

- *Fair value of common stock.* See the subsection titled “—Determination of Fair Value of Common Stock” below.
- *Expected term.* The expected term represents the weighted-average period the stock options are expected to remain outstanding and is based on the options’ vesting terms and contractual terms as we do not have sufficient historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior.
- *Expected volatility.* As the Company did not have sufficient trading history of its common stock, the expected volatility was estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable industry peers were chosen based on their size, stage of their life cycle or area of specialty. We will continue to apply this process until enough historical information regarding the volatility of our stock price becomes available.
- *Risk-free interest rate.* The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.
- *Expected dividend yield.* We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

The Company has also granted stock options with graded vesting based on market, service and performance conditions. At the grant date, the fair value of these stock options was estimated using a Monte Carlo simulation model, which uses a distribution of potential outcomes over the vesting period. The assumptions utilized in the calculation included the Company’s expected common stock price, expected volatility, risk-free rate and expected term. Stock-based compensation expense for these awards is recognized on a straight-line basis over the requisite service period, which is the longer of the explicit service period of the service condition and the derived service period of the market condition, as determined for each separately vesting portion of the awards as if each award was, in substance, multiple awards.

We account for forfeitures of stock-based awards as they occur rather than applying an estimated forfeiture rate to stock-based compensation expense.

We recorded stock-based compensation expense of \$19.5 million and \$8.6 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, there was unrecognized stock-based compensation expense of \$54.4

million related to unvested stock options, which we expect to recognize over a remaining weighted-average period of 2.5 years. We expect to continue to grant equity-based awards in the future, and to the extent that we do, our stock-based compensations expense recognized in future periods will likely increase.

See Note 10 to our consolidated financial statements in Part II, Item 8. of this Annual Report on Form 10-K for additional information about the assumptions we used to determine the estimated fair value of our stock options granted in the periods presented.

Determination of Fair Value of Common Stock

Prior to our IPO, the fair value of our common stock underlying our share-based awards was determined by our board of directors with assistance from management and external valuation experts. The approach in estimating the fair value of our common stock was consistent with the methods outlined in the American Institute of Certified Public Accountants Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the “Practice Aid”).

In addition to considering the results of independent third-party valuations, we considered various objective and subjective factors to determine the fair value of common stock as of each grant date, including:

- the prices at which we sold shares of our preferred stock and the superior rights, preferences and privileges of our preferred stock relative to those of our common stock at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies and clinical trials for our product candidates;
- our stage of development and our business strategy, and material risks related to our business;
- external market conditions affecting the biotechnology industry and trends within the biotechnology industry;
- the competitive landscape for our product candidates;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an IPO or a sale of our company, given prevailing market conditions; and
- the economy in general.

Prior to May 2023, we utilized an Option Pricing Method (“OPM”) based analysis, primarily the OPM backsolve methodology, to determine the estimated fair value of our common stock. Within the OPM framework, we determined the backsolve method was the most appropriate method for determining the fair value of our common stock. The backsolve method is used for inferring the total equity value implied by a recent financing transaction, or by an estimated equity value of our pipeline product candidates, involves the construction of an allocation model that takes into account our capital structure and the rights, preferences and privileges of each class of stock, then assumes reasonable inputs for the other OPM variables (expected time to liquidity, volatility and risk-free rate). The total equity value is then iterated in the model until the model output value for the equity class sold in a recent financing round equals the price paid in that round. The OPM is generally utilized when specific future liquidity events are difficult to forecast (i.e., the enterprise has many choices and options available), and the enterprise’s value depends on how well it follows an uncharted path through the various possible opportunities and challenges. The resulting equity value was then assigned to each class of equity securities using the OPM, which treats ordinary shares and preferred shares as call options on the equity value, with

exercise prices based on the liquidation preference of our preferred stock. The shares of common stock are modeled as a call option with a claim on the equity value at an exercise price equal to the remaining value immediately after our preferred stock is liquidated. After the equity value was determined and allocated to the various classes of equity securities, we applied discounts to reflect the lack of marketability of our common stock based on the weighted-average expected time to liquidity. The estimated fair value of the common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

For valuations performed in or after May 2023, and before June 27, 2024, we utilized a hybrid method that combined the Probability-Weighted Expected Return Method (“PWERM”), an accepted valuation method described in the Practice Aid, and the OPM. We determined this was the most appropriate method for determining the fair value of our common stock based on our stage of development and other relevant factors. The PWERM is a scenario-based analysis that estimates the value per share of common stock based on the probability-weighted present value of expected future equity values for the common stock, under various possible future liquidity event scenarios, considering the rights and preferences of each class of shares, discounted for a lack of marketability. Under the hybrid method, an OPM was utilized to determine the fair value of our common stock in certain of the PWERM scenarios (capturing situations where our development path and future liquidity events were difficult to forecast), potential exit events were explicitly modeled in the other PWERM scenarios. A discount for lack of marketability was applied to the value derived under each scenario to account for a lack of access to an active public market to estimate our common stock fair value. We also considered the amount of time between the independent third-party valuation dates and the grant dates and performed an interpolation of the fair value between the two valuation dates to estimate common stock fair value at each grant date. This determination included an evaluation of whether the subsequent valuation indicated that any significant change in valuation had occurred between the previous valuation and the grant date.

The assumptions underlying these valuations represented management’s best estimate, which involved inherent uncertainties and the application of management’s judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could be materially different.

Once a public trading market for our common stock was established in connection with our IPO, it was no longer necessary for our board of directors to estimate the fair value of our common stock in connection with accounting for granted stock options and other such awards we may grant, as the fair value of our common stock was based on the IPO price per share and thereafter on our publicly traded common stock price, as listed on the Nasdaq Global Select Market under the ticker “ALMS.”

Derivative Liability

We determined that the obligation to issue additional shares of redeemable convertible preferred stock upon the occurrence of certain events, including our board of directors’ consent, represented a freestanding financial instrument. The instrument was classified as a liability in the consolidated balance sheets prior to the IPO and was subject to re-measurement at each balance sheet date and at the settlement date. Any change in fair value was recognized in the statements of operations and comprehensive loss.

We utilized the Black-Scholes option pricing model, which incorporates assumptions and estimates, to value the derivative liability. On a quarterly basis, we assessed these assumptions and estimates as additional information impacting the assumptions was obtained. Significant estimates and assumptions impacting fair value included the estimated time and probability of closing of the second tranche financing, preferred stock fair value and estimated stock volatility.

We determined the fair value per share of the underlying redeemable convertible preferred stock by taking into consideration our most recent sales of our preferred stock as well as additional factors that we deemed relevant. We were a private company and lacked company-specific historical and implied volatility information of our stock. Therefore, we determined expected stock volatility based on the historical volatility of the prices of shares of common stock of publicly traded peer companies. We estimated the risk-free interest rate by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the outstanding tranche liability. We assumed a 0% dividend considering that our board of directors had no history of declaring dividends and did not intend to declare any.

In May 2023, we estimated the fair value of the derivative liability of \$2.1 million at the issuance date. We recognized changes in fair value of \$0.1 million as other expense in the consolidated statement of operations and comprehensive loss in the year ended December 31, 2023. The derivative liability was settled in October 2023, when investors purchased shares of Series B-2 and Series B-2A redeemable convertible preferred stock in a second tranche closing.

In connection with the Series C redeemable convertible preferred stock financings in March 2024 and May 2024, we issued to investors two freestanding financial instruments and estimated their fair value of \$8.9 million at the issuance date. The derivative liability was re-measured at fair value of \$14.3 million and was settled in May 2024, when we closed the second tranche of the Series C financing. The change in fair value of derivative liability was recognized in other income (expense), net in the consolidated statement of operations and comprehensive loss in the year ended December 31, 2024.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

JOBS Act Transition Period and Smaller Reporting Company Status

We are an “emerging growth company” as defined in the JOBS Act. Under the JOBS Act, an emerging growth company can take advantage of the extended transition period for complying with new or revised accounting standards and delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption from complying with new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation exemptions to the requirements for (i) providing an auditor’s attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board (the “PCAOB”) regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an emerging growth company until the earlier to occur of (a) the last day of the fiscal year (A) following the fifth anniversary of the completion of our IPO, (B) in which we have total annual gross revenues of at least \$1.235 billion or (C) in which we are deemed to be a “large accelerated filer” under the rules of the SEC, which means the market value of our common stock and non-voting common stock that is held by non-affiliates exceeds \$700.0 million as of the prior June 30th, or (b) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

We are also a “smaller reporting company,” meaning that the market value of our common stock and non-voting common stock held by non-affiliates plus the aggregate amount of gross proceeds expected from our IPO was less than \$700.0 million as of June 30, 2024, and our annual revenue was less than \$100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our common stock and non-voting common stock held by non-affiliates is less than \$250.0 million or (ii) our annual revenue is less than \$100.0 million during the most recently completed fiscal year and the market value of our common stock and non-voting common stock held by non-affiliates is less than \$700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

The primary objectives of our investment activities are to ensure liquidity and to preserve capital. We are exposed to market risks related to changes in interest rates of our cash equivalents and marketable securities. However, due to the nature of these cash equivalents and marketable securities, we do not believe that a hypothetical 10% increase or decrease in interest rates during any of the periods presented would have had a material effect on our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Foreign Currency Exchange Risk

All of our employees and our operations are currently located in the United States, and our expenses are generally denominated in U.S. dollars. However, we do utilize certain CRO and CMO vendors outside of the United States for our clinical trials and product development and manufacturing. As such, our expenses are denominated in both U.S. dollars and foreign currencies. Therefore, our operations are and will continue to be subject to fluctuations in foreign currency exchange rates. To date, foreign currency transaction gains and losses have not been material to our consolidated financial statements, and we have not had a formal hedging program with respect to foreign currency. We do not believe that a hypothetical 10% increase or decrease in exchange rates during any of the periods presented would have had a material effect on our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and research and development costs. We do not believe that inflation had a material effect on our business, results of operations, or financial condition, or on our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Item 8. Financial Statements and Supplementary Data

ALUMIS INC.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Alumis Inc.

Opinion on the Financial Statements

We have audited the accompanying 2024 financial statements of Alumis Inc. and the 2023 consolidated financial statements of Alumis Inc. and its subsidiaries (collectively referred to as the “Company”), which comprise the balance sheets as of December 31, 2024 and 2023, and the related statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders’ equity (deficit) and of cash flows for the years then ended, including the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt About the Company’s Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred negative operating cash flows and significant losses from operations since its inception that raise substantial doubt about its ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

We conducted our audits of these financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 19, 2025

We have served as the Company’s auditor since 2022.

ALUMIS INC.
CONSOLIDATED BALANCE SHEETS

| (in thousands, except share and per share amounts) | December 31, 2024 | December 31, 2023 |
|---|------------------------------|------------------------------|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$ 169,526 | \$ 45,996 |
| Restricted cash | — | 113 |
| Marketable securities | 118,737 | 2,956 |
| Research and development prepaid expenses | 13,424 | 2,661 |
| Other prepaid expenses and current assets | 4,501 | 1,631 |
| Total current assets | 306,188 | 53,357 |
| Restricted cash, non-current | 1,106 | 1,024 |
| Property and equipment, net | 20,968 | 22,441 |
| Operating lease right-of-use assets, net | 12,723 | 12,783 |
| Other long-term assets | 7 | 7 |
| Total assets | <u>\$ 340,992</u> | <u>\$ 89,612</u> |
| Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit) | | |
| Current liabilities: | | |
| Accounts payable | \$ 9,624 | \$ 1,118 |
| Research and development accrued expenses | 29,149 | 10,946 |
| Other accrued expenses and current liabilities | 10,580 | 7,087 |
| Operating lease liabilities, current | 1,557 | 1,720 |
| Total current liabilities | 50,910 | 20,871 |
| Operating lease liabilities, non-current | 29,165 | 30,860 |
| Share repurchase liability | 813 | 1,771 |
| Total liabilities | <u>80,888</u> | <u>53,502</u> |
| Commitments and contingencies (Note 7) | | |
| Redeemable convertible preferred stock, \$0.0001 par value; zero and 89,016,578 shares authorized as of December 31, 2024 and 2023, respectively; zero and 85,960,088 shares issued and outstanding as of December 31, 2024 and 2023, respectively; aggregate liquidation preference of zero and \$370,540 as of December 31, 2024 and 2023, respectively | — | 375,370 |
| Stockholders' equity (deficit): | | |
| Preferred stock, \$0.0001 par value; 50,000,000 shares authorized, zero shares issued and outstanding as of December 31, 2024; zero shares authorized, issued and outstanding as of December 31, 2023 | — | — |
| Common stock, voting, \$0.0001 par value; 492,815,092 and 125,000,000 voting shares authorized as of December 31, 2024 and 2023, respectively; 47,222,419 and 2,675,979 voting shares issued and outstanding as of December 31, 2024 and 2023, respectively | 4 | 1 |
| Common stock, non-voting, \$0.0001 par value; 7,184,908 and 85,960,088 non-voting shares authorized as of December 31, 2024 and 2023, respectively; 7,184,908 and zero non-voting shares issued and outstanding as of December 31, 2024 and 2023, respectively | 1 | — |
| Additional paid-in capital | 918,610 | 25,055 |
| Accumulated other comprehensive income (loss) | 40 | 2 |
| Accumulated deficit | (658,551) | (364,318) |
| Total stockholders' equity (deficit) | <u>260,104</u> | <u>(339,260)</u> |
| Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit) | <u>\$ 340,992</u> | <u>\$ 89,612</u> |

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

ALUMIS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

| (in thousands, except share and per share amounts) | Year Ended December 31, | |
|---|--------------------------------|---------------------|
| | 2024 | 2023 |
| Operating expenses: | | |
| Research and development expenses, including related party expenses of \$912 and \$1,519 for the years ended December 31, 2024 and 2023, respectively | \$ 265,554 | \$ 137,676 |
| General and administrative expenses | 35,200 | 20,498 |
| Total operating expenses | <u>300,754</u> | <u>158,174</u> |
| Loss from operations | (300,754) | (158,174) |
| Other income (expense): | | |
| Interest income | 12,020 | 3,368 |
| Change in fair value of derivative liability | (5,406) | (119) |
| Other income (expenses), net | (93) | (68) |
| Total other income (expense), net | <u>6,521</u> | <u>3,181</u> |
| Net loss | <u>\$ (294,233)</u> | <u>\$ (154,993)</u> |
| Other comprehensive income (loss): | | |
| Unrealized gain (loss) on marketable securities, net | 38 | 129 |
| Net loss and other comprehensive loss | <u>\$ (294,195)</u> | <u>\$ (154,864)</u> |
| Net loss per share attributable to common stockholders, basic and diluted | <u>\$ (10.38)</u> | <u>\$ (72.08)</u> |
| Weighted-average shares of common stock outstanding, basic and diluted | <u>28,341,866</u> | <u>2,150,186</u> |

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

ALUMIS INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND
STOCKHOLDERS' EQUITY (DEFICIT)

| (in thousands, except share amounts) | Redeemable Convertible Preferred Stock | | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Accumulated Deficit | Total Stockholders' Equity (Deficit) |
|---|--|-------------------|-------------------|-------------|----------------------------|---|---------------------|--------------------------------------|
| | Shares | Amount | Shares | Amount | | | | |
| Balance as of December 31, 2022 | 67,960,088 | \$ 285,473 | 2,642,334 | \$ 1 | \$ 14,209 | \$ (127) | \$ (209,325) | \$ (195,242) |
| Issuance of Series B-2 and B-2A redeemable convertible preferred stock in May 2023 for cash, net of derivative liability of \$2,112 and offering costs of \$208 | 12,000,000 | 57,679 | — | — | — | — | — | — |
| Issuance of Series B-2 and B-2A redeemable convertible preferred stock in October 2023 for cash, net of offering costs of \$13, and settlement of derivative liability of \$2,231 | 6,000,000 | 32,218 | — | — | — | — | — | — |
| Issuance of common stock upon exercise of stock options and early exercise of stock options | — | — | 48,442 | — | 277 | — | — | 277 |
| Vesting of early exercised stock options | — | — | — | — | 1,921 | — | — | 1,921 |
| Vesting of restricted shares of common stock | — | — | — | — | 23 | — | — | 23 |
| Repurchase of unvested early exercised stock options | — | — | (14,797) | — | — | — | — | — |
| Stock-based compensation expense | — | — | — | — | 8,625 | — | — | 8,625 |
| Other comprehensive loss, net | — | — | — | — | — | 129 | — | 129 |
| Net loss | — | — | — | — | — | — | (154,993) | (154,993) |
| Balance as of December 31, 2023 | 85,960,088 | 375,370 | 2,675,979 | 1 | 25,055 | 2 | (364,318) | (339,260) |
| Issuance of Series C redeemable convertible preferred stock in March 2024 for cash, net of derivative liability of \$8,913 and offering costs of \$382 | 41,264,891 | 120,205 | — | — | — | — | — | — |
| Issuance of Series C redeemable convertible preferred stock in May 2024 for cash and settlement of the derivative liability of \$14,319, net of offering costs of \$157 | 41,264,892 | 143,662 | — | — | — | — | — | — |
| Issuance of voting common stock upon initial public offering, net of underwriting discounts and commissions and other offering costs of \$16,684 | — | — | 13,125,000 | 1 | 193,315 | — | — | 193,316 |
| Issuance of voting common stock in private placement transaction | — | — | 2,500,000 | — | 40,000 | — | — | 40,000 |
| Conversion and redesignation of redeemable convertible preferred stock into 28,855,656 shares of voting common stock and 7,184,908 shares of non-voting common stock in connection with initial public offering | (168,489,871) | (639,237) | 36,040,564 | 3 | 639,234 | — | — | 639,237 |
| Issuance of common stock upon exercise of stock options and early exercise of stock options | — | — | 72,201 | — | 375 | — | — | 375 |
| Vesting of early exercised stock options | — | — | — | — | 1,154 | — | — | 1,154 |
| Vesting of restricted shares of common stock | — | — | — | — | 20 | — | — | 20 |
| Repurchase of unvested early exercised restricted common stock | — | — | (6,417) | — | — | — | — | — |
| Stock-based compensation expense | — | — | — | — | 19,457 | — | — | 19,457 |
| Other comprehensive income, net | — | — | — | — | — | 38 | — | 38 |
| Net loss | — | — | — | — | — | — | (294,233) | (294,233) |
| Balance as of December 31, 2024 | — | \$ — | 54,407,327 | \$ 5 | \$ 918,610 | \$ 40 | \$ (658,551) | \$ 260,104 |

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

ALUMIS INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

| (in thousands, except share amounts) | Year ended December 31. | |
|--|-------------------------|------------------|
| | 2024 | 2023 |
| Cash flows from operating activities | | |
| Net loss | \$ (294,233) | \$ (154,993) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Stock-based compensation | 19,457 | 8,625 |
| Change in fair value of derivative liability | 5,406 | 119 |
| Net accretion of discounts on marketable securities | (3,685) | (544) |
| Depreciation and amortization | 3,152 | 1,284 |
| Non-cash lease expense | 60 | 2,010 |
| Loss on disposal of fixed assets | 5 | 266 |
| Write-off of deferred offering costs | — | 555 |
| Loss on abandonment of right-of-use assets | — | 645 |
| Changes in operating assets and liabilities: | | |
| Research and development prepaid expenses | (10,763) | 5,526 |
| Other prepaid expenses and other assets | (2,870) | (340) |
| Accounts payable | 8,506 | (642) |
| Research and development accrued expenses | 18,203 | 5,168 |
| Other accrued expenses and current liabilities | 3,542 | 2,490 |
| Operating lease liabilities | (1,858) | (144) |
| Net cash used in operating activities | <u>(255,078)</u> | <u>(129,975)</u> |
| Cash flows from investing activities | | |
| Maturities of marketable securities | 128,000 | 76,250 |
| Purchases of marketable securities | (240,058) | (11,279) |
| Purchases of property and equipment | (1,732) | (4,499) |
| Net cash (used in) provided by investing activities | <u>(113,790)</u> | <u>60,472</u> |
| Cash flows from financing activities | | |
| Proceeds from issuance of redeemable convertible preferred stock and derivative liability, net of offering costs | 258,461 | 89,778 |
| Proceeds from initial public offering, net of underwriter discounts and commissions and other offering costs | 193,316 | — |
| Proceeds from a private placement transaction | 40,000 | — |
| Proceeds from issuance of common stock upon exercise of stock options | 596 | 453 |
| Payments of deferred offering costs | — | (485) |
| Repurchase of unvested common stock shares issued upon early exercised stock options | (6) | (64) |
| Net cash provided by financing activities | <u>492,367</u> | <u>89,682</u> |
| Net increase in cash, cash equivalents and restricted cash | 123,499 | 20,179 |
| Cash, cash equivalents and restricted cash at beginning of period | 47,133 | 26,954 |
| Cash, cash equivalents and restricted cash at end of period | <u>\$ 170,632</u> | <u>\$ 47,133</u> |
| Supplemental disclosures: | | |
| Conversion of 168,489,871 shares of redeemable convertible preferred stock upon the closing of initial public offering | \$ 639,237 | \$ — |
| Settlement of derivative liability upon issuance of redeemable convertible preferred stock | \$ (14,319) | \$ (2,231) |
| Recognition of derivative liability upon issuance of redeemable convertible preferred stock | \$ 8,913 | \$ 2,112 |
| Vesting of early exercised stock options and unvested restricted shares of common stock | \$ 1,174 | \$ 1,944 |
| Right-of-use assets obtained in exchange for operating lease liabilities | \$ — | \$ 14,255 |
| Property and equipment acquired through tenant improvement allowance | \$ — | \$ 16,691 |
| Purchases of property and equipment in other accrued expenses and current liabilities | \$ — | \$ 49 |
| Reconciliation of cash, cash equivalents and restricted cash: | | |
| Cash and cash equivalents | \$ 169,526 | \$ 45,996 |
| Restricted cash | — | 113 |
| Restricted cash, non-current | 1,106 | 1,024 |
| Total cash, cash equivalents and restricted cash | <u>\$ 170,632</u> | <u>\$ 47,133</u> |

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

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Nature of the Business

Organization and Business

Alumis Inc. (the “Company”) is a clinical stage biopharmaceutical company focused on identifying, acquiring, and accelerating the development and commercialization of transformative medicines for autoimmune disorders. The Company leverages its proprietary precision data analytics platform, biological insights, and a team of experts with deep experience in precision medicine drug discovery, development, and immunology, to create medicines that significantly improve the lives of patients by replacing broad immunosuppression with targeted therapies.

The Company was founded on January 29, 2021, as a Delaware corporation under the name FL2021-001, Inc. FL2021-001, Inc.’s name was changed to Esker Therapeutics, Inc. on March 8, 2021 and to Alumis Inc. on January 6, 2022. The Company is headquartered in South San Francisco, California.

As of December 31, 2023, the Company had two wholly owned subsidiaries, FronThera U.S. Holdings, Inc. and FronThera U.S. Pharmaceuticals LLC. FronThera U.S. Holdings, Inc. was dissolved on April 8, 2024 and FronThera U.S. Pharmaceuticals LLC was dissolved on March 14, 2024. These subsidiaries did not have operations during the years ended December 31, 2024 and 2023.

Reverse Stock Split

On June 19, 2024, the board of directors approved, and on June 20, 2024, the Company effected, a reverse stock split of the shares of the Company’s outstanding common stock at a ratio of 1-for-4.675 (the “Reverse Stock Split”). The number of authorized shares and par value per share were not adjusted as a result of the Reverse Stock Split. All references to shares, options to purchase common stock, share amounts, per share amounts, and related information contained in the audited consolidated financial statements have been retrospectively adjusted to reflect the effect of the Reverse Stock Split for all periods presented. The shares of common stock underlying outstanding stock options and other equity instruments were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the agreements governing such securities. In addition, the conversion ratios for each series of the Company’s redeemable convertible preferred stock, which were automatically convertible into shares of common stock upon the closing of the Company’s initial public offering (“IPO”) of common stock, were proportionally adjusted.

IPO and Concurrent Private Placement

On June 27, 2024, the Company’s Registration Statement on Form S-1 for its IPO was declared effective, and on July 1, 2024, the Company completed its IPO, pursuant to which it issued and sold 13,125,000 shares of its common stock at \$16.00 price per share to the public. Net proceeds from the IPO were \$193.3 million, after deducting underwriting discounts and commissions and other offering costs totaling \$16.7 million.

In connection with the IPO, an existing investor and a holder of more than 5% of the Company’s capital stock, purchased an additional 2,500,000 shares of the Company’s common stock at the IPO price per share for total gross and net proceeds of \$40.0 million in a private placement transaction (the “Concurrent Private Placement”). The closing of the Concurrent Private Placement was contingent on the closing of the IPO. The sale of such shares is not registered under the Securities Act of 1933, as amended (the “Securities Act”), and as such, the shares may not be offered or sold absent registration or an applicable exemption from registration. The shares sold in connection with the Concurrent Private Placement are subject to existing resale registration rights and were subject to a 180-day lock-up agreement with the underwriters in the IPO that expired on December 24, 2024. The Concurrent Private Placement closed on July 17, 2024.

Immediately prior to the closing of the IPO on July 1, 2024, all of the shares of the Company’s redeemable convertible preferred stock then outstanding converted into 28,855,656 shares of Class A common stock and 7,184,908 shares of Class B common stock at a 1-for-4.675 conversion ratio (the “Preferred Stock Conversion”). All outstanding Class A common stock shares and all outstanding Class B common stock shares were redesignated immediately thereafter into the same

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

number of shares of voting common stock and non-voting common stock, respectively (the “Common Stock Reclassification”).

In connection with the closing of the Company’s IPO, the Company increased the authorized number of shares to 500,000,000 shares of common stock and 50,000,000 shares of preferred stock. The authorized number of common stock shares includes voting common stock of 492,815,092 shares and non-voting common stock of 7,184,908 shares.

Unless the context otherwise requires a different meaning, all references to “common stock” in these notes refers to the Company’s voting common stock and non-voting common stock combined.

Liquidity and Going Concern

The Company has incurred negative operating cash flows and significant losses from operations since its inception. For the years ended December 31, 2024 and 2023, the Company incurred net losses of \$294.2 million and \$155.0 million, respectively. Cash used in operating activities was \$255.1 million and \$130.0 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, the Company had an accumulated deficit of \$658.6 million.

The Company has historically financed its operations primarily through issuance of common stock, redeemable convertible preferred stock and convertible promissory notes in private placements, and most recently, through its IPO and Concurrent Private Placement. The Company expects to continue to incur substantial losses for the foreseeable future, and its ability to achieve and sustain profitability will depend on the successful development, approval, and commercialization of any product candidates it may develop, and on the achievement of sufficient revenue to support its cost structure. The Company may never achieve profitability and, unless and until it does, it will need to continue to raise additional capital. The Company believes that, based on its current operating plan, its existing cash, cash equivalents and marketable securities of \$288.3 million as of December 31, 2024, will not be sufficient to meet its operating and capital requirements for at least 12 months from the date of issuance of these consolidated financial statements and there is substantial doubt about the Company’s ability to continue as a going concern.

In February 2025, the Company entered into a Merger Agreement (as defined in Note 15) through an all-stock transaction that would improve the Company’s liquidity. However, as of the date of the issuance of these consolidated financial statements, the Merger has not been completed and there can be no assurance that it will be consummated. The Company will need to raise significant additional capital to fund ongoing research and development activities and maintain future operations. The Company’s management plans to monitor expenses and may raise additional capital through a combination of public and private equity, debt financings, strategic alliances, and licensing arrangements. The Company’s ability to access capital when needed is not assured and, if capital is not available to the Company when, and in the amounts, needed, on the terms which are favorable, the Company could be required to delay, scale back, or abandon some or all of its planned development programs and other operations, which could materially harm the Company’s business, financial condition and results of operations.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The accompanying consolidated financial statements do not reflect any adjustments relating to the recoverability and reclassifications of assets and liabilities that might be necessary if the Company is unable to continue as a going concern.

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

2. Summary of Significant Accounting Policies and Basis of Presentation

Basis of Presentation

The accompanying consolidated financial statements and accompanying notes have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”). Prior to their dissolution, the Company’s consolidated financial statements included the accounts of FronThera U.S. Holdings Inc. and FronThera U.S. Pharmaceuticals LLC, two wholly owned subsidiaries, and all intercompany transactions were eliminated.

Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”).

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period.

On an ongoing basis, the Company evaluates estimates and assumptions, including but not limited to those related to accruals for research and development expenses and accruals, stock-based compensation expense, the fair value of common stock and the fair value of the derivative liability. Management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from those estimates.

Segment and Geographical Information

The Company operates and manages its business as one reportable and operating segment, which is the business of researching and developing medicines for autoimmune disorders. The chief executive officer, who is the chief operating decision maker (“CODM”), reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance (see Note 14). All of the Company’s long-lived assets are located in the United States.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentration of credit risk, consist primarily of cash and cash equivalents, investments in marketable securities and restricted cash. The Company maintains bank deposits in federally insured financial institutions and certain of these deposits exceed federally insured limits. To date, the Company has not experienced any losses on its deposits of cash and periodically evaluates the creditworthiness of the financial institutions at which its bank deposits are maintained.

The Company may also invest in money market funds, U.S. treasuries, commercial paper, corporate bonds, supranational debt securities and agency bonds, which can be subject to certain credit risks. The Company mitigates the risks by investing in high-grade instruments, limiting its exposure to any one issuer and monitoring the ongoing creditworthiness of the financial institutions and issuers. The Company has not experienced any loss of principal on its financial instruments.

Risks and Uncertainties

The Company is subject to certain risks and uncertainties, including, but not limited to, changes in any of the following areas that the Company believes could have a material adverse effect on the future financial position or results of operations: the Company’s ability to advance the development of its proprietary precision data analytics platform, timing and ability to advance its product candidates through preclinical and clinical development; costs and timelines associated

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

with the manufacturing of clinical supplies; regulatory approval, market acceptance of, and reimbursement for, any product candidates the Company may develop; performance of third-party vendors; competition from pharmaceutical or other biotechnology companies with greater financial resources or expertise; protection of intellectual property; litigation or claims against the Company based on intellectual property or other factors; and its ability to attract and retain employees necessary to support its growth.

The Company's business and results of operations may be affected by worldwide economic conditions, which may continue to be impacted by global macroeconomic challenges and uncertainty in the markets, including severely diminished liquidity and credit availability, rising inflation and monetary supply shifts, rising interest rates, labor shortages, declines in consumer confidence, declines in economic growth, increases in unemployment rates, recession risks and uncertainty about economic and geopolitical stability (for example, related to the ongoing conflicts in Ukraine and Israel and the surrounding areas). These worldwide economic conditions may continue into 2025 and may negatively impact the Company's business, financial position and results of operations.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents.

Restricted Cash

Restricted cash represents security deposits in the form of letters of credit issued in connection with the Company's leases (see Note 7).

Marketable Securities

Marketable securities may consist of money market funds, U.S. treasuries, commercial paper, corporate bonds, supranational debt securities and agency bonds with original maturities of more than three months at the time of purchase. As the Company's entire investment portfolio is considered available for use in current operations, the Company classifies all marketable securities as available-for-sale and as current assets, even though the stated maturity may be more than one year from the current balance sheet date. Marketable securities are carried at fair value, with change in fair value reported as unrealized gains or losses in accumulated other comprehensive income (loss), which is a separate component of stockholders' equity (deficit) in the consolidated balance sheets.

The amortized cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income in the consolidated statements of operations and comprehensive loss. Realized gains and losses on the sale of securities are determined by specific identification of each security's cost basis. The Company regularly reviews its investment portfolio to determine if any security is impaired, which would require it to record an allowance for credit losses or an impairment charge in the period any such determination is made. In making this judgment, the Company evaluates, among other things, the extent to which the fair value of a security is less than its amortized cost, its intent to sell or whether it is more likely than not that the Company will be required to sell the security before recovery of its amortized cost basis, the financial condition of the issuer and any changes thereto, and, as necessary, the portion of a decline in fair value that is credit-related. This assessment could change in the future due to new developments or changes in assumptions related to any particular security. Realized gains and losses, allowances for credit losses and impairments on available-for-sale marketable securities, if any, are recorded in the consolidated statements of operations and comprehensive loss.

Fair Value Measurement

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The carrying amounts of prepaid expenses, other current assets, accounts payable, accrued expenses and other liabilities approximate fair value due to their short-term maturities.

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

instruments, such as money market funds, marketable securities and derivative liabilities are measured at fair value at each reporting date (see Note 3).

Deferred Offering Costs

Deferred offering costs, consisting of legal, accounting and other third-party fees directly relating to in-process equity financings or offerings are capitalized. Deferred offering costs are offset against offering proceeds upon the completion of the financing or the offering. In the event the financing or the offering is terminated or delayed, deferred offering costs are expensed immediately as a charge to general and administrative expenses in the consolidated statements of operations and comprehensive loss. As of December 31, 2024 and 2023, the Company had no deferred offering costs in its consolidated balance sheets.

Property and Equipment, net

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of assets. Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated once placed into service. Repair and maintenance costs that are not considered improvements and do not extend the useful life of property and equipment, are expensed as incurred. Improvements are capitalized as additions to property and equipment. Upon sale or retirement of assets, the costs and related accumulated depreciation are removed from the consolidated balance sheets and the resulting gain or loss is reflected within operating expenses in the consolidated statements of operations and comprehensive loss.

Asset Acquisitions and Acquired In-Process Research and Development Expenses

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the asset or group of assets, which includes transaction costs. The Company determines if the acquisition should be accounted for as an asset acquisition after considering whether substantially all of the fair value of the gross assets acquired is concentrated in a single asset or group of assets and whether the Company acquired a substantive process capable of significantly contributing to the Company's ability to create outputs. Goodwill is not recognized in asset acquisitions. If acquired in-process technology assets, including licenses, know-how and patents are determined to not have an alternative future use, the cost is charged to research and development expenses at the acquisition date.

The Company accounts for contingent consideration identified in an asset acquisition that does not meet the definition of a derivative under ASC 815, *Derivatives and Hedging*, when the payment becomes probable and reasonably estimable.

Such amounts are expensed or capitalized based on the nature of the associated asset at the date the related contingency is recognized.

Leases

The Company determines whether an arrangement is or contains a lease at the inception of the arrangement and whether such a lease should be classified as a financing lease or operating lease at the commencement date of the lease. Leases with a term greater than one year are classified as operating lease right-of-use assets, net and operating lease liabilities, current and non-current in the consolidated balance sheets. The Company elected not to recognize the right-of-use assets and lease liabilities for leases with lease terms of one year or less (short-term leases). Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the lease term. The Company considers the lease term to be the noncancelable period that it has the right to use the underlying asset, together with any periods where it is reasonably certain it will exercise an option to extend (or not terminate) the lease. As the interest rate implicit in the Company's lease contracts is not readily determinable, the Company utilizes its incremental borrowing rate to determine the present value of lease payments. The incremental borrowing rate is derived from information available at the lease commencement date and represents the rate of interest that a lessee would have to pay to borrow an amount equal to the lease payments on a collateralized basis over a similar term in a similar economic environment.

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Rent expense for operating leases is recognized on a straight-line basis over the lease term. The Company has elected to not separate lease and non-lease components for its real estate leases and instead accounts for each separate lease component and the non-lease components associated with that lease component as a single lease component. Variable lease payments are recognized as incurred.

As of December 31, 2024 and 2023, the Company had no finance leases.

Impairment of Long-Lived Assets

The Company regularly reviews the carrying value and estimated lives of all of its long-lived assets, including property and equipment, and ROU assets to determine whether indicators of impairment may exist which warrant adjustments to carrying values or estimated useful lives. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset group to future undiscounted net cash flows expected to be generated by the asset or asset group. Should impairment exist, the impairment loss to be recognized is measured by the amount by which the carrying amount of the asset exceeds the projected discounted future net cash flows arising from the asset.

Derivative Liability

The Company may issue financial instruments, such as promissory notes, which include embedded derivatives, such as call options. Derivatives are accounted for under ASC 815, *Derivatives and Hedging*. The Company performs analysis of derivatives embedded in the financial instruments, and if any requires bifurcation, accounts for these at fair value at the issuance date. In May 2024, the Company issued Series C redeemable convertible preferred stock shares, which included embedded derivatives that required bifurcation (see Note 3).

A derivative liability is accounted for separately from the financial instrument at fair value on the issuance date and is remeasured each reporting period. The changes in the fair value of the derivative liability are included in change in fair value of derivative liability in the consolidated statements of operations and comprehensive loss.

Redeemable Convertible Preferred Stock

The Company recorded redeemable convertible preferred stock at their respective fair values on the dates of issuance, net of offering costs. The redeemable convertible preferred stock was recorded outside of permanent equity because while it was not mandatory, redemption was contingent upon the occurrence of certain events considered not solely within the Company's control. The Company did not adjust the carrying values of the redeemable convertible preferred stock to the liquidation preferences of such stock, because it was uncertain whether or when a deemed liquidation event would occur that would obligate the Company to pay the liquidation preferences to holders of redeemable convertible preferred stock. Subsequent adjustments to the carrying values to the liquidation preferences would be made only when it became probable that such a deemed liquidation event would occur (see Note 8).

Research and Development Expenses and Accruals

Research and development costs are expensed as incurred. Research and development costs consist primarily of costs associated with acquiring technology and intellectual property licenses that have no alternative future uses, costs incurred under in-license or assignment agreements, salaries and benefits of research and development personnel, costs related to research activities, preclinical studies, clinical trials, drug manufacturing, third-party professional research and development consulting services, and allocated overhead and facility-related expenses. Payments associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate future use will also be expensed as incurred.

The Company records accrued liabilities for estimated costs of its research and development activities conducted by third-party service providers. The Company accrues these costs based on factors such as estimates of the work completed and in accordance with the third-party service agreements. If the Company does not identify costs that have begun to be

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incurred or if the Company underestimates or overestimates the level of services performed or the costs of these services, actual expenses could differ from the estimates. To date, the Company has not experienced any material differences between accrued costs and actual costs incurred.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed and classified as current or non-current prepaid expenses and other assets.

The Company makes payments in connection with clinical trials to CMOs that manufacture the materials for its product candidates and to CROs and clinical trial sites that conduct and manage the Company's clinical trials. The financial terms of these contracts are subject to negotiation, which vary by contract and may result in payments that do not match the periods over which materials or services are provided. Generally, these agreements set forth the scope of work to be performed at a fixed fee, unit price or on a time and materials basis. The Company makes estimates of accrued research and development expenses as of each balance sheet date based on facts and circumstances known at that time. The Company periodically confirms the accuracy of its estimates with the service providers and makes adjustments, if necessary. Research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development services provided, but not yet invoiced, are included in accrued expenses in the consolidated balance sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Stock-Based Compensation

The Company grants stock-based awards to employees, directors and non-employee consultants in the form of stock options to purchase shares of its common stock. The Company measures stock options granted with service-based vesting based on the fair value of the award on the grant date using the Black-Scholes option-pricing model. The model requires management to make a number of assumptions, including common stock fair value, expected volatility, expected term, risk-free interest rate and expected dividend yield. The Company expenses the fair value of its stock-based compensation awards on a straight-line basis over the requisite service period, which is the period in which the related services are received.

The Company has also granted stock options with graded vesting based on market, service and performance conditions. At the grant date, the fair value of these stock options was estimated using a Monte Carlo simulation model, which uses a distribution of potential outcomes over the vesting period. The assumptions utilized in the calculation included the Company's expected common stock price, expected volatility, risk-free rate and expected term. Stock-based compensation expense for these awards is recognized on a straight-line basis over the requisite service period, which is the longer of the explicit service period of the service condition and the derived service period of the market condition, as determined for each separately vesting portion of the awards as if each award was, in substance, multiple awards.

The Company accounts for award forfeitures as they occur. The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's salary or services costs are classified.

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Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes.

The Company assesses the likelihood of deferred tax assets being realized. It provides a valuation allowance when it is more likely than not that some portion or all of a deferred tax asset 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.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Tax positions that meet the more-likely-than-not threshold are measured at the largest amount of tax benefit that is greater than 50% likely of being realized upon settlement with the taxing authority. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Comprehensive Loss

Comprehensive loss represents all changes in stockholders' deficit except those resulting from distributions to stockholders. The Company's other comprehensive income (loss) for the years ended December 31, 2024 and 2023 consisted of unrealized gain (loss) on marketable securities, net of taxes.

Net Loss Per Share Attributable to Common Stockholders

Basic and diluted net loss per share attributable to common stockholders is presented in conformity with the two-class method required for participating securities. As such, net income is attributed to common stockholders and participating securities based on their participation rights. Prior to the IPO, under the two-class method, the net loss attributable to common stockholders was not allocated to the redeemable convertible preferred stock as the holders of the redeemable convertible preferred stock did not have a contractual obligation to share in the Company's losses. Upon the IPO, the Company's redeemable convertible preferred stock converted into either Class A or Class B common stock, and were immediately thereafter redesignated into voting and non-voting common stock, respectively, and therefore are included in the allocation of net loss attributable to common stockholders as they share in the Company's losses. Voting and non-voting common stock participate in the Company's losses equally. Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock and potentially dilutive securities outstanding for the period. Potentially dilutive securities include common stock issued and outstanding, unvested restricted common stock, early exercised stock options, and redeemable convertible preferred stock issued and outstanding. As the Company has reported losses for all periods presented, all potentially dilutive securities are antidilutive and accordingly, basic net loss per share equals diluted net loss per share.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. The Company qualifies as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"), and has elected not to "opt out" of the extended transition related to complying with new or revised accounting standards, which means that when a standard is issued or revised and it has different application dates for public and private companies, the Company will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that the

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Company either (i) irrevocably elects to “opt out” of such extended transition period or (ii) no longer qualifies as an emerging growth company. The Company may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* (“ASU 2023-07”). This ASU requires public entities to disclose information about their reportable segments’ significant expenses and other segment items on an interim and annual basis. Public entities with a single reportable segment are required to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in ASC 280 on an interim and annual basis. ASU 2023-07 is effective for fiscal years beginning after December 15, 2023, and for interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. The Company adopted this standard in the consolidated financial statements for the year ended December 31, 2024. The adoption of this standard did not impact the Company’s reportable segments and additional required disclosures have been included in Note 14.

In March 2024, the FASB issued ASU No. 2024-02, *Codification Improvements - Amendments to Remove References to the Concepts Statements* (“ASU 2024-02”). ASU 2024-02 clarifies and simplifies references to certain concept statements within U.S. GAAP and applies to all reporting entities within the scope of the affected accounting guidance, but in most instances the references removed are extraneous and not required to understand or apply the guidance. ASU 2024-02 is effective for fiscal years beginning after December 15, 2024 for public entities and for fiscal years beginning after December 15, 2025 for all other entities, with early application permitted. The Company adopted this standard in the consolidated financial statements for the year ended December 31, 2024. The adoption of this standard did not have a material impact on its consolidated financial statements at the adoption date.

Recently Issued and Not Yet Adopted Accounting Pronouncements

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* (“ASU 2023-09”), which requires the disclosure of specific categories in the rate reconciliation and greater disaggregation for income taxes paid. ASU 2023-09 is effective for annual periods beginning after December 15, 2024 for public entities and for fiscal years beginning after December 15, 2025 for all other entities, with early application permitted. ASU 2023-09 should be adopted prospectively with the option to be adopted retrospectively. The Company is currently evaluating the impact of this standard on its disclosure in its consolidated financial statements.

In November 2024, the FASB issued ASU No. 2024-03, *Disaggregation of Income Statement Expenses (Topic 220)* (“ASU 2024-03”), requiring that public business entities disclose additional information about specific expense categories in the notes to financial statements at interim and annual reporting periods. The amendments of ASU 2024-03 are effective for annual reporting periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. The requirements of ASU 2024-03 may be applied either prospectively to financial statements issued for reporting periods after the effective date or retrospectively to any or all prior periods presented in the financial statements. The Company is currently evaluating the impact of adopting ASU 2024-03 on its consolidated financial statements and disclosures.

3. Fair Value Measurements

The Company discloses and recognizes the fair value of its assets and liabilities using a hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The guidance establishes three levels of the fair value hierarchy as follows:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for

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substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company’s assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. The Company recognizes transfers into and out of levels within the fair value hierarchy in the period in which the actual event or change in circumstances that caused the transfer occurs.

The Company’s financial instruments consist of Level 1, Level 2 and Level 3 financial instruments. Changes in the ability to observe valuation inputs may result in a reclassification of levels of certain securities within the fair value hierarchy.

Level 1 financial instruments are comprised of money market funds and U.S. treasuries. Level 2 financial instruments are comprised of U.S. treasuries. Usually, short term marketable securities are considered Level 2 when their fair values are determined using inputs that are observable in the market or can be derived principally from or corroborated by observable market data such as pricing for similar securities, recently executed transactions, cash flow models with yield curves, and benchmark securities. In addition, Level 2 financial instruments are valued using comparisons to like-kind financial instruments and models that use readily observable market data as their basis. Level 3 financial instruments include derivative liabilities issued in May 2023 and settled in October 2023 in connection with the closing of the second tranche of the Series B-2 and B-2A redeemable convertible preferred stock financing, and issued in March 2024 and settled in May 2024 in connection with the closing of the second tranche of the Series C redeemable convertible preferred stock financing.

The following tables represent the Company’s fair value hierarchy for financial assets measured at fair value on a recurring basis as of December 31, 2024 and 2023 (in thousands):

| | Fair Value Measurements as of December 31, 2024 | | | |
|------------------------------|---|------------------|-------------|-------------------|
| | Level 1 | Level 2 | Level 3 | Total |
| Assets: | | | | |
| Cash equivalents | | | | |
| Money market funds | \$ 168,847 | \$ — | \$ — | \$ 168,847 |
| Marketable securities | | | | |
| U.S. treasuries | 47,137 | 71,600 | — | 118,737 |
| Total assets | <u>\$ 215,984</u> | <u>\$ 71,600</u> | <u>\$ —</u> | <u>\$ 287,584</u> |

| | Fair Value Measurements as of December 31, 2023 | | | |
|------------------------------|---|---------------|-------------|------------------|
| | Level 1 | Level 2 | Level 3 | Total |
| Assets: | | | | |
| Cash equivalents | | | | |
| Money market funds | \$ 21,310 | \$ — | \$ — | \$ 21,310 |
| U.S. treasuries | 2,000 | — | — | 2,000 |
| Marketable securities | | | | |
| U.S. treasuries | 1,958 | 998 | — | 2,956 |
| Total assets | <u>\$ 25,268</u> | <u>\$ 998</u> | <u>\$ —</u> | <u>\$ 26,266</u> |

The derivative liability issued in May 2023 in connection with the closing of the second tranche of the Series B-2 and B-2A redeemable convertible preferred stock financing was a freestanding financial instrument and represented the Company’s obligation to issue additional shares of Series B-2 and B-2A redeemable convertible preferred stock at a fixed price upon the approval by the Company’s board of directors. In connection with the Series C redeemable convertible preferred stock financing in March 2024, the Company issued to investors two freestanding financial instruments: the

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Series C second tranche option liability and the put right option liability. The Company estimated their fair value using a Black-Scholes option-pricing model weighted by the probability of occurring. The Company used the intrinsic value calculation to estimate the fair value of the Series C second tranche option liability and the put right option liability upon settlement.

The following table provides a range of assumptions used in the valuation of the derivative liability for the years ended December 31, 2024 and 2023:

| | Year Ended December 31, | |
|--------------------------------|-------------------------|-----------------|
| | 2024 | 2023 |
| Expected term (in years) | 0.2 – 0.4 | 0.0 – 0.4 |
| Volatility | 55.1% – 59.9 % | 43.2% – 83.2 % |
| Risk-free interest rate | 5.4% – 5.5% % | 5.2% – 5.6 % |
| Dividend yield | 0.0 % | 0.0 % |
| Probability of option exercise | 0.0% – 100.0% % | 30.0% – 100.0 % |

The following table provides a roll-forward of the fair value of the Company's Level 3 financial instruments, the derivative liability, for the years ended December 31, 2024 and 2023 (in thousands):

| | Year Ended December 31, | |
|-----------------------------------|-------------------------|---------|
| | 2024 | 2023 |
| Fair value at beginning of period | \$ — | \$ — |
| Fair value upon issuance | 8,913 | 2,112 |
| Changes in fair value | 5,406 | 119 |
| Fair value upon settlement | (14,319) | (2,231) |
| Fair value at end of period | \$ — | \$ — |

There were no transfers between Level 1, Level 2 or Level 3 categories for the years ended December 31, 2024 and 2023.

4. Marketable Securities

Marketable securities, which are classified as available-for-sale, consisted of the following as of December 31, 2024 and 2023 (in thousands):

| | Amortized Cost Basis | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value as of December 31, 2024 |
|--|-------------------------|------------------------------|-------------------------------|--|
| Short-term marketable securities: | | | | |
| U.S. treasuries | \$ 118,697 | \$ 45 | \$ (5) | \$ 118,737 |
| Total short-term marketable securities | \$ 118,697 | \$ 45 | \$ (5) | \$ 118,737 |

| | Amortized Cost Basis | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value as of December 31, 2023 |
|--|-------------------------|------------------------------|-------------------------------|--|
| Short-term marketable securities: | | | | |
| U.S. treasuries | \$ 2,954 | \$ 2 | \$ — | \$ 2,956 |
| Total short-term marketable securities | \$ 2,954 | \$ 2 | \$ — | \$ 2,956 |

All marketable securities held as of December 31, 2024 and 2023 had contractual maturities of less than one year.

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As of December 31, 2024 and 2023, no significant facts or circumstances were present to indicate a deterioration in the creditworthiness of the issuers of the marketable securities, and the Company has no requirement or intention to sell these securities before maturity or recovery of their amortized cost basis. The Company considered the current and expected future economic and market conditions and determined that its marketable securities were not significantly impacted. For all marketable securities with a fair value less than its amortized cost basis, the Company determined the decline in fair value below amortized cost basis to be immaterial and non-credit related, and therefore no allowance for expected credit losses was recorded. For the years ended December 31, 2024 and 2023, the Company did not recognize any impairment losses on its marketable securities.

5. Balance Sheet Components

Other Prepaid Expenses and Current Assets

Other prepaid expenses and current assets consisted of the following as of December 31, 2024 and 2023 (in thousands):

| | December 31, 2024 | December 31, 2023 |
|---|----------------------|----------------------|
| Prepaid insurance | \$ 695 | \$ 111 |
| Prepaid subscriptions | 1,232 | 703 |
| Interest receivable | 698 | 108 |
| Tax receivable | 1,114 | 614 |
| Other | 762 | 95 |
| Total other prepaid expenses and current assets | <u>\$ 4,501</u> | <u>\$ 1,631</u> |

Property and Equipment, net

Property and equipment, net consisted of the following as of December 31, 2024 and 2023 (in thousands):

| | Estimated Useful Life (in years) | December 31, 2024 | December 31, 2023 |
|---|---|----------------------|----------------------|
| Leasehold improvements | Shorter of useful life or lease term | \$ 17,618 | \$ 17,592 |
| Laboratory equipment | 5 | 5,227 | 3,577 |
| Furniture and fixtures | 5 | 1,709 | 1,709 |
| Computer equipment | 5 | 896 | 896 |
| Capitalized software | 3 | 75 | 75 |
| Total property and equipment, gross | | <u>25,525</u> | <u>23,849</u> |
| Less: Accumulated depreciation and amortization | | <u>(4,557)</u> | <u>(1,408)</u> |
| Total property and equipment, net | | <u>\$ 20,968</u> | <u>\$ 22,441</u> |

Depreciation and amortization expense was \$3.2 million and \$1.3 million for the years ended December 31, 2024 and 2023, respectively.

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Other Accrued Expenses and Current Liabilities

Other accrued expenses and current liabilities consisted of the following as of December 31, 2024 and 2023 (in thousands):

| | December 31, 2024 | December 31, 2023 |
|--|----------------------|----------------------|
| Accrued personnel and related expenses | \$ 7,765 | \$ 5,585 |
| Accrued professional services | 2,657 | 1,093 |
| Accrued other expenses | 158 | 409 |
| Total other accrued expenses and current liabilities | <u>\$ 10,580</u> | <u>\$ 7,087</u> |

6. Related Party Transactions**Foresite Labs Services Agreement**

Foresite Labs, LLC (“Foresite Labs”) is an affiliate of Foresite Capital Management, a stockholder of the Company. In January 2021, the Company entered into a services agreement with Foresite Labs, which was amended and restated in August 2021 and in December 2023, and expires in December 2026, unless terminated earlier by the parties. Thereafter, on each anniversary of the effective date, the agreement will automatically renew for an additional one-year term, unless terminated earlier by the parties. Foresite Labs provides services to assist the Company in exploring specified immunology genetic targets. For the years ended December 31, 2024 and 2023, the Company recognized \$0.9 million and \$1.5 million as research and development expenses under the service agreement, respectively. Accrued expenses under the service agreement were zero and \$2 thousand as of December 31, 2024 and 2023, respectively.

7. Commitments and Contingent Liabilities**Operating Leases**

In 2021, the Company entered into a lease agreement for 14,000 square feet of office space in South San Francisco, California, which commenced in August 2021 and had a contractual termination date of September 2024. In September 2023, the Company abandoned this right-of-use asset as it had moved to its new office space described below; the Company recognized a loss on this abandonment in the amount of \$0.6 million.

In January 2022, the Company entered into a lease agreement for 12,000 square feet of office and laboratory space in South San Francisco, California, which commenced in July 2022 and had a contractual termination date of July 2029. This lease contained an early termination option, allowing the Company to terminate this lease before the expiry of the lease term. The Company concluded the lease term for accounting purposes ended in August 2023. In April 2023, the lease was modified, and the contractual lease termination was changed to October 2023. The accounting impact of the modification was not material.

In August 2022, the Company entered into a lease agreement for 55,000 square feet of office and laboratory space in South San Francisco, California, which commenced in January 2023 and has a contractual termination date in August 2033. The Company constructed leasehold improvements in the space, which were concluded to be lessee assets. The lessor provided the Company a tenant improvement allowance of \$17.2 million, of which \$0.5 million and \$16.7 million were received and were accounted for as a reduction to lease payments for the years ended December 31, 2022 and 2023, respectively. At the commencement date, future lease payments totaled \$37.9 million, including \$54.6 million in gross fixed payments less \$16.7 million in lease incentives received during the first year of the lease. The lease liability at lease commencement was calculated to be \$14.1 million, which is equal to the present value of the future lease payments, discounted at the incremental borrowing rate of 11.4%. Following the commencement date, the Company measured its lease liability and right-of-use asset in accordance with ASC 842-20-35-3. In accordance with this guidance, future lease payments increased as the \$16.7 million incentive was received, and future gross fixed payments were no longer offset by these incentives. Leasehold improvements were reflected in property and equipment, net in the consolidated balance sheets as of

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December 31, 2024 and 2023. The lease agreement also includes a renewal option allowing the Company to extend this lease for an additional three years at the prevailing rental rate, which the Company was not reasonably certain to exercise.

In December 2024, the Company entered into a lease agreement for approximately 22,000 square feet of additional office space in South San Francisco, California. The lease has a contractual termination date of December 2026, with the right to extend the lease for an additional two years subject to certain conditions. The Company determined that, for accounting purposes, the commencement date of the lease is in January 2025 and the lease term ends in December 2026, as it not reasonably certain that the lease will be extended. Therefore, the Company will recognize the right-of-use asset and the lease liability on the commencement date in January 2025. Total undiscounted lease payments over the lease term will be approximately \$1.9 million.

The Company maintains letters of credit representing security deposits on its leases in the amount of \$1.1 million as of December 31, 2024 and 2023. The letters of credit were reflected in restricted cash, non-current in the consolidated balance sheets as of December 31, 2024 and in restricted cash, current and non-current in the consolidated balance sheets as of December 31, 2023.

The components of lease costs were as follows (in thousands):

| | Year Ended December 31, | |
|-----------------------|-------------------------|-----------------|
| | 2024 | 2023 |
| Operating lease costs | \$ 3,469 | \$ 4,747 |
| Variable lease costs | 1,202 | 545 |
| Total lease costs | <u>\$ 4,671</u> | <u>\$ 5,292</u> |

Supplemental cash flow information related to the operating leases were as follows (in thousands):

| | Year Ended December 31, | |
|--|-------------------------|----------|
| | 2024 | 2023 |
| Cash payments included in the measurement of operating lease liabilities | \$ 5,299 | \$ 2,903 |

Weighted-average remaining lease term and incremental borrowing rate for the operating leases were as follows:

| | December 31, 2024 | December 31, 2023 |
|---|----------------------|----------------------|
| Weighted-average remaining lease term (years) | 8.7 | 9.5 |
| Weighted-average incremental borrowing rate | 11.4 % | 11.4 % |

Future minimum lease payments under non-cancelable leases as of December 31, 2024 were as detailed below (in thousands):

| | |
|-----------------------------------|------------------|
| 2025 | \$ 4,959 |
| 2026 | 5,125 |
| 2027 | 5,296 |
| 2028 | 5,474 |
| 2029 | 5,658 |
| Thereafter | 21,857 |
| Total undiscounted lease payments | <u>48,369</u> |
| Less: Imputed interest | (17,647) |
| Total operating lease liabilities | <u>\$ 30,722</u> |

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FronThera Contingent Consideration

In March 2021, the Company entered into a stock purchase agreement to acquire FronThera U.S. Holdings, Inc. and its wholly owned subsidiary, FronThera U.S. Pharmaceuticals LLC., and the transaction was accounted for as an asset acquisition. Under the stock purchase agreement, the Company is obligated to pay contingent consideration of up to an aggregate of \$120.0 million based on the achievement of specified clinical and approval milestones, of up to an aggregate of \$70.0 million payable for clinical milestones, and of up to an aggregate of \$50.0 million payable for approval milestones, all related to technology acquired under the agreement. In the year ended December 31, 2022, the Company incurred and made a \$37.0 million milestone payment for the first administration of ESK-001 to a patient enrolled in a Phase 2 clinical trial of ESK-001, which was recorded in research and development expenses in the consolidated statements of operations and comprehensive loss. In July 2024, the Company met a milestone in connection with the first administration of ESK-001 to a patient enrolled in a Phase 3 clinical trial of ESK-001 and made a \$23.0 million milestone payment in August 2024, which was recorded in research and development expenses in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2024. No other milestones were achieved or were probable of being achieved as December 31, 2024.

Research and Development Agreements

The Company enters into various agreements in the ordinary course of business, such as those with suppliers, CROs, CMOs and clinical trial sites. These agreements provide for termination at the request of either party, generally with less than one-year notice and are, therefore, cancellable contracts and, if cancelled, are not anticipated to have a material effect on the Company's financial condition, results of operations, or cash flows.

Legal Contingencies

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of business. The Company records a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount. Management is currently not aware of any legal matters that could have a material adverse effect on the Company's financial position, results of operations or cash flows.

Guarantees and Indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. Its exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To the extent permitted under Delaware law, the Company has agreed to indemnify its directors and officers for certain events or occurrences while the director or officer is, or was serving, at a request in such capacity. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2024 and 2023, the Company did not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

8. Redeemable Convertible Preferred Stock

In May 2023, the Company issued and sold an aggregate of 10,722,340 shares of Series B-2 redeemable convertible preferred stock for gross proceeds of \$53.6 million and 1,277,660 shares of Series B-2A redeemable convertible preferred stock for gross proceeds of \$6.4 million and incurred \$0.2 million of offering costs. The purchase price for Series B-2 and B-2A redeemable convertible preferred stock was \$5.00 per share. The Series B-2 and Series B-2A stock purchase agreement contained an obligation to issue additional shares of Series B-2 or Series B-2A redeemable convertible preferred stock in a second tranche closing by October 2023 (the "Second Tranche Series B-2 Closing") upon the occurrence of certain events, including the board of directors' consent. The Company recognized this call option as a derivative liability and estimated its fair value of \$2.1 million.

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In July 2023, the holders of the shares of Series B-2A redeemable convertible preferred stock elected to convert their 1,277,660 shares into the same number of Series B-2 redeemable convertible preferred stock.

In October 2023, the Company closed the Second Tranche Series B-2 Closing and issued an additional 4,221,170 shares of Series B-2 redeemable convertible preferred stock and 1,778,830 shares of Series B-2A redeemable convertible preferred stock at a price of \$5.00 per share and received gross proceeds of \$21.1 million and \$8.9 million, respectively. Accordingly, the derivative liability was settled, and the Company reclassified the derivative liability, remeasured at fair value of \$2.2 million, into redeemable convertible preferred stock. The Company incurred less than \$0.1 million of offering costs in connection with the Second Tranche Series B-2 Closing.

In March 2024, the Company issued and sold an aggregate of 41,264,891 shares of Series C redeemable convertible preferred stock for gross proceeds of \$129.5 million and incurred \$0.4 million of offering costs. The purchase price for Series C redeemable convertible preferred stock was \$3.13826 per share. Under the Series C stock purchase agreement, any time prior to the earliest of (i) December 31, 2024, (ii) the execution of a letter of intent for the sale of the Company, or (iii) the closing date of the Company's IPO, at the discretion of the Company's board of directors, the Company was obligated to sell and each Series C purchaser was obligated to purchase additional shares of Series C redeemable convertible preferred stock with the amount equal to the purchaser's aggregate purchase price in the first tranche Series C closing less any previous payments by the purchaser as part of the Put Right (as defined below) exercise. If the purchaser did not purchase its full share in the second tranche closing (the "Second Tranche Series C Closing"), all of its existing shares of Series C redeemable convertible stock and Series C-1 redeemable convertible preferred stock were convertible into voting common stock at a 10-to-1 basis. Additionally, a purchaser had a right to purchase shares of Series C-1 redeemable convertible preferred stock at a purchase price of \$4.00 per share beginning from the earlier of (a) September 4, 2024 or (b) the date of a significant partnering or collaboration agreement and expiring upon the earlier of (a) December 31, 2024, (b) the public filing of a registration statement on Form S-1 for the IPO, (c) the Second Tranche Series C Closing and (d) the execution of a letter of intent for the sale of the Company (the "Put Right"). The Put Right could only be exercised once. The Company determined that the Second Tranche Series C Closing and the Put Right were two freestanding financial instruments and recognized the derivative liabilities at their estimated fair value of \$8.9 million at the issuance date.

In May 2024, the Company closed the Second Tranche Series C Closing and issued an additional 41,264,892 shares of Series C redeemable convertible preferred stock at a price of \$3.13826 per share. The Company received gross proceeds of \$129.5 million and incurred \$0.2 million of offering costs. Accordingly, the derivative liabilities were settled, and the Company reclassified the derivative liabilities, remeasured at fair value of \$14.3 million, into redeemable convertible preferred stock.

Immediately prior to the closing of the Company's IPO on July 1, 2024, all outstanding shares of the Company's redeemable convertible preferred stock were converted and then redesignated into voting and non-voting common stock (see Note 1) and are no longer outstanding.

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The Company's redeemable convertible preferred stock as of December 31, 2023, consisted of the following:

| | December 31, 2023 | | | |
|--|----------------------|--|--|-----------------------|
| | Shares Authorized | Shares Issued and Outstanding <small>(in thousands, except share amounts)</small> | Aggregate Liquidation Preference | Net Carrying Value |
| Series Seed redeemable convertible preferred stock | 10,500,000 | 10,500,000 | \$ 10,500 | \$ 10,480 |
| Series A redeemable convertible preferred stock | 7,500,000 | 7,500,000 | 30,000 | 29,972 |
| Series B redeemable convertible preferred stock | 40,200,000 | 40,200,000 | 201,000 | 200,711 |
| Series B-1 redeemable convertible preferred stock | 9,760,088 | 9,760,088 | 39,040 | 44,310 |
| Series B-2 redeemable convertible preferred stock | 18,000,000 | 16,221,170 | 81,106 | 80,969 |
| Series B-2A redeemable convertible preferred stock | 3,056,490 | 1,778,830 | 8,894 | 8,928 |
| Total redeemable convertible preferred stock | <u>89,016,578</u> | <u>85,960,088</u> | <u>\$ 370,540</u> | <u>\$ 375,370</u> |

9. Stockholders' Equity (Deficit)

As of December 31, 2023, the Company was authorized to issue 125,000,000 shares of Class A common stock and 85,960,088 shares of Class B common stock, both with par values of \$0.0001 per share.

In June 2024, the Company's board of directors approved the amended and restated certificate of incorporation, which was filed upon the closing of the IPO and which authorized the Company to issue up to 50,000,000 shares of preferred stock, with a par value of \$0.0001 per share, and 492,815,092 shares of voting common stock and 7,184,908 shares of non-voting common stock, both with par values of \$0.0001 per share.

Immediately prior to the closing of the IPO on July 1, 2024, all of the shares of the Company's redeemable convertible preferred stock then outstanding converted 28,855,656 shares of Class A common stock and 7,184,908 shares of Class B common stock at a 1-for-4.675 conversion ratio. All outstanding Class A common stock shares and all outstanding Class B common stock shares were redesignated immediately thereafter into the same number of shares of voting common stock and non-voting common stock, respectively.

As of December 31, 2024, there were no shares of preferred stock issued or outstanding, and 47,222,419 and 7,184,908 shares of voting common stock and non-voting common stock, respectively, outstanding.

The holders of voting and non-voting common stock have the same rights except that non-voting common stock does not have voting rights, except as may be required by law. Each holder of non-voting common stock has a right to convert each share of non-voting common stock to one share of voting common stock subject to the following limitations. At any time following the Company's registration of any class of equity securities under the Exchange Act, the holders of shares of non-voting common stock may not convert a number of shares of non-voting common stock into shares of voting common stock in excess of that number of shares of non-voting common stock which would cause the holder thereof to beneficially own (for purposes of Section 13(d) of the Exchange Act), in excess of 4.99% of the total number of issued and outstanding shares of voting common stock. Such maximum percentage may be increased or decreased to such other percentage as any holder of outstanding shares of non-voting common stock may designate in writing (in the case of an increase upon 61 days' prior written notice).

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Common stock reserved for issuance, on an as-converted basis, consisted of the following as of December 31, 2024 and 2023:

| | December 31, 2024 | December 31, 2023 |
|--|--------------------------|--------------------------|
| Outstanding and issued stock options | 9,458,788 | 5,096,086 |
| Shares available for grant under 2024 Equity Incentive Plan | 6,893,517 | — |
| Shares available for grant under 2024 Employee Stock Purchase Plan | 650,000 | — |
| Shares available for grant under 2024 Performance Option Plan | 92,800 | — |
| Shares available for grant under 2021 Stock Plan | — | 296,189 |
| Redeemable convertible preferred stock issued and outstanding | — | 18,387,168 |
| Total | <u>17,095,105</u> | <u>23,779,443</u> |

Common Stock Issued to Executives

In February 2021, the Company issued 100,532 shares of restricted common stock to two executives at a purchase price of \$0.94 per share. The shares vest over a four-year period with a one-year cliff vesting. The holders have voting and dividends rights. The Company has the right to repurchase unvested shares of common stock at the price paid by the holder in the event of termination of the holder’s continuous status as a service provider. The Company estimated the fair value of the restricted stock awards based on the fair value of common stock at the grant dates. The expense is recognized ratably over the vesting terms. The Company recognized \$0.1 million of stock-based compensation expense related to restricted stock awards for each of the years ended December 31, 2024 and 2023. In the year ended December 31, 2024, a holder’s continuous service terminated, and the Company repurchased the unvested shares.

The following table summarizes the activity for the Company’s restricted common stock for the years ended December 31, 2024 and 2023:

| | Number of Shares | Weighted- Average Grant Date Fair Value |
|----------------------------------|---------------------|--|
| Unvested as of December 31, 2023 | 29,322 | \$ 2.90 |
| Vested | (20,322) | \$ 2.90 |
| Repurchased | (6,417) | \$ 2.90 |
| Unvested as of December 31, 2024 | <u>2,583</u> | \$ 2.90 |

As of December 31, 2024, the remaining unamortized stock-based compensation expense was immaterial.

10. Stock-Based Compensation

2021 Stock Plan

In February 2021, the Company adopted its 2021 Stock Plan (the “2021 Plan”), which provided for stock awards to eligible employees, directors and consultants of the Company. Awards issuable under the 2021 Plan included incentive stock options (“ISOs”), non-statutory stock options (“NSOs”), restricted stock units (“RSUs”) and stock grants. Subsequent to the adoption of the 2024 Equity Incentive Plan (the “2024 EIP”) in June 2024, described below, no additional shares were available for issuance under the 2021 Plan, and any stock options granted under the 2021 Plan that were subsequently forfeited would be made available for issuance under the 2024 EIP.

The terms of the 2021 Plan permit option holders to exercise options before their options are vested. The shares of common stock granted upon early exercise that have not yet vested are subject to repurchase by the Company in the event of termination of the holder’s continuous status as a service provider, at the price paid by the holder.

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Stock Option Repricing

In March 2024, the Company's board of directors approved the repricing of all outstanding options as of March 29, 2024, which had an exercise price exceeding \$8.84 per share. The exercise price of outstanding options with a weighted average exercise price of \$10.23 for 4,603,443 common stock shares was reduced to the estimated common stock fair value of \$8.84 per share at the date of the repricing. The vesting terms and expiration dates remain unchanged from the original grant dates.

The stock option repricing was treated as an option modification for accounting purposes and resulted in total incremental expense of \$0.7 million, of which \$0.1 million incremental expense associated with the vested options was recognized on the modification date. The remaining \$0.6 million incremental expense associated with the unvested options as of the modification date is being recognized over the remainder of the original requisite service period.

2024 Performance Option Plan

In May 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 Performance Option Plan (the "2024 POP"). The Company reserved 1,880,680 shares of common stock issuable under the 2024 POP. The 2024 POP permits grants of ISOs, NSOs and restricted stock awards to the Company's employees, directors and consultants.

In May 2024, the Company granted NSOs to employees to purchase 1,880,680 shares of common stock at an exercise price of \$10.19 under the 2024 POP. Options generally vest on the date when the Company meets certain common stock public market price specified targets after the end of the lock-up period, subject to continuous service through each respective vest date. The price targets are calculated based on the volume weighted average price per share over 30 consecutive trading dates, in accordance with the grant terms. The unvested awards will expire if it is determined that the vesting conditions have not been met during the applicable six-year performance period. The service condition includes monthly vesting over 36 months from the vesting commencement date and the employee's continuous service with the Company through each such monthly vesting date. The terms of the 2024 POP permit option holders to exercise options before their options are vested, if the market condition has been met.

2024 Equity Incentive Plan

In June 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 EIP, which became effective on June 27, 2024, upon execution of the underwriting agreement related to the Company's IPO. The Company reserved 7,800,000 new shares of common stock for issuance under the 2024 EIP. In addition, up to 6,829,339 shares subject to awards under the 2021 Plan that terminate, expire, or lapse for any reason without the delivery of shares, or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price, were authorized to be added to the 2024 EIP. The 2024 EIP also provides that the number of shares initially reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2025 through January 1, 2034, by an amount equal to 5% of the outstanding number of shares of the Company's common stock as of the last day of the immediately preceding fiscal year, or such lesser number of shares as determined by the board of directors prior to the applicable January 1. No more than 43,888,017 shares of common stock may be issued upon the exercise of incentive stock options under the 2024 EIP.

The 2024 EIP allows the Company to make equity-based awards to its officers, employees, directors and consultants. The 2024 EIP provides for the grant of ISOs, NSOs, restricted stock awards, RSUs, stock appreciation rights, performance awards and other stock-based awards. Options under the 2024 EIP may be granted for periods of up to 10 years at exercise prices no less than the fair market value of common stock on the date of grant; provided, however, that the exercise price of an incentive stock option granted to a 10% stockholder may not be less than 110% of the fair market value of the shares on the date of grant and such option may not be exercisable after the expiration of five years from the date of grant. Stock option grants under the 2024 EIP generally vest over four years. The grant date fair market value of all awards made under the 2024 EIP and all cash compensation paid by the Company to any non-employee director for services as a director in any fiscal year may not exceed \$750,000, or increased to \$1,000,000 in the fiscal year of their initial service as a non-

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employee director. The terms of the 2024 EIP do not permit option holders to exercise options before their options are vested.

2024 Employee Stock Purchase Plan

In June 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 Employee Stock Purchase Plan (the "2024 ESPP"), which became effective on June 28, 2024, upon execution of the underwriting agreement related to the Company's IPO. The Company reserved 650,000 shares of common stock for issuance under the 2024 ESPP. The number of shares of common stock reserved for issuance under the 2024 ESPP will be automatically increased each year for ten calendar years beginning on January 1, 2025 through January 1, 2034, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (ii) 1,950,000 shares; provided that before the date of any such increase, the board of directors may determine that such increase will be less than the amount in (i) and (ii) above. The 2024 ESPP allows an eligible employee to purchase shares of common stock at an amount equal to 85% of the lower of the fair market value of the Company's common stock at the beginning of the offering period or at each applicable purchase date during an offering period as established by the board of directors. In December 2024, the Company's board of directors approved the grant of purchase rights under an offering period beginning on January 24, 2025.

Stock Option Activity

2021 Plan and 2024 EIP

The following table summarizes the Company's stock option activity under the 2021 Plan and 2024 EIP for the years ended December 31, 2024 and 2023. The table includes early exercised shares as part of stock options exercised.

| | Options | Weighted-Average Exercise Price Per Share | Weighted- Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value (in thousands) |
|--|------------------|--|--|---|
| Outstanding as of December 31, 2023 | 5,096,086 | \$ 9.68 | 8.5 | \$ 15,033 |
| Granted | 2,902,385 | \$ 11.68 | | |
| Exercised | (72,201) | \$ 8.26 | | \$ 333 |
| Forfeited or expired | (255,362) | \$ 10.23 | | |
| Outstanding, vested and expected to vest as of December 31, 2024 | <u>7,670,908</u> | \$ 9.59 | 8.2 | \$ 1,777 |
| Exercisable as of December 31, 2024 | <u>6,565,317</u> | \$ 9.31 | 8.0 | \$ 1,777 |

Total exercisable shares of 6,565,317 as of December 31, 2024 included 3,906,969 unvested shares that were early exercisable under the 2021 Plan.

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2024 POP

The following table summarizes the Company's stock option activity under the 2024 POP for the year ended December 31, 2024.

| | Options | Weighted-Average Exercise Price Per Share | Weighted-Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value (in thousands) |
|--|------------------|---|--|--|
| Outstanding as of December 31, 2023 | — | \$ — | — | \$ — |
| Granted | 1,880,680 | \$ 10.19 | | |
| Forfeited or expired | (92,800) | \$ 10.19 | | |
| Outstanding, vested and expected to vest as of December 31, 2024 | <u>1,787,880</u> | \$ 10.19 | 9.3 | \$ — |
| Exercisable as of December 31, 2024 | <u>—</u> | \$ — | — | \$ — |

Valuation of Stock Options Granted Under the 2021 Plan and 2024 EIP

The weighted-average grant date fair value of stock options granted under the 2021 Plan and the 2024 EIP for the years ended December 31, 2024 and 2023 was \$9.92 and \$10.93 per stock option, respectively. The total fair value of stock options vested for the years ended December 31, 2024 and 2023 was \$5.8 million and \$8.1 million, respectively.

The fair value of these stock options was estimated using the Black-Scholes option pricing model with the following assumptions:

| | Year Ended December 31, | |
|--------------------------|-------------------------|-------------------|
| | 2024 | 2023 |
| Expected term (in years) | 5.8 – 6.1 | 5.8 – 6.6 |
| Volatility | 103.65% – 109.78 % | 97.65% – 102.54 % |
| Risk-free interest rate | 3.47% – 4.48 % | 3.66% – 4.77 % |
| Dividend yield | 0.00 % | 0.00 % |

Expected Term

The expected term represents the weighted-average period the stock options are expected to remain outstanding and is based on the options' vesting terms and contractual terms as the Company does not have sufficient historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior.

Expected Volatility

The expected stock price volatility assumption was determined by examining the historical volatilities for industry peers, as the Company did not have sufficient trading history of its common stock. The Company will continue to use industry peers in determining historical stock price volatility until sufficient historical data of its common stock becomes available.

Risk-Free Interest Rate

The risk-free interest rate assumption is based on the U.S. Treasury instruments whose term was consistent with the expected term of the Company's stock options.

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Dividends

The Company has not paid any cash dividends on common stock since inception and does not anticipate paying any dividends in the foreseeable future. Consequently, an expected dividend yield of zero was used.

Common Stock Fair Value

Prior to the IPO, the fair market value of the Company's common stock was determined by the board of directors with assistance from management and external valuation experts. The approach to estimating the fair market value of common stock was consistent with the methods outlined in the Practice Aid.

Prior to May 2023, the Company utilized an Option Pricing Method ("OPM") based analysis, primarily the OPM backsolve methodology, to determine the estimated fair value of the common stock. Within the OPM framework, the backsolve method, for inferring the total equity value implied by a recent financing transaction or by an estimated equity value of the Company's pipeline product candidates, involves the construction of an allocation model that takes into account the Company's capital structure and the rights, preferences and privileges of each class of stock, then assumes reasonable inputs for the other OPM variables (expected time to liquidity, volatility, and risk-free rate). The total equity value is then iterated in the model until the model output value for the equity class sold in a recent financing round equals the price paid in that round. The OPM is generally utilized when specific future liquidity events are difficult to forecast (i.e., the enterprise has many choices and options available), and the enterprise's value depends on how well it follows an uncharted path through the various possible opportunities and challenges. In determining the estimated fair value of the common stock, the board of directors also considered the fact that the stockholders could not freely trade the common stock in the public markets. Accordingly, the Company applied discounts to reflect the lack of marketability of its common stock based on the weighted-average expected time to liquidity. The estimated fair value of the common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

For valuations performed between May 2024 and before June 27, 2024, the Company utilized a hybrid method that combined the Probability-Weighted Expected Return Method ("PWERM"), an accepted valuation method described in the Practice Aid, and the OPM. The Company determined this was the most appropriate method for determining the fair value of its common stock based on the stage of development and other relevant factors. The PWERM is a scenario-based analysis that estimates the value per share of common stock based on the probability-weighted present value of expected future equity values for the common stock, under various possible future liquidity event scenarios, considering the rights and preferences of each class of shares, discounted for a lack of marketability. Under the hybrid method, an OPM was utilized to determine the fair value of the Company's common stock in certain of the PWERM scenarios (capturing situations where its development path and future liquidity events were difficult to forecast), potential exit events were explicitly modeled in the other PWERM scenarios. A discount for lack of marketability was applied to the value derived under each scenario to account for a lack of access to an active public market to estimate the common stock fair value.

The Company also considered the amount of time between the independent third-party valuation dates and the grant dates and performed an interpolation of the fair value between the two valuation dates to estimate common stock fair value at each grant date. This determination includes an evaluation of whether the subsequent valuation indicated that any significant change in valuation had occurred between the previous valuation and the grant date.

The assumptions underlying these valuations represented management's best estimates, which involved inherent uncertainties and the application of management's judgment. As a result, if the Company had used significantly different assumptions or estimates, the fair value of the common stock and the stock-based compensation expense could have been materially different.

Once a public trading market for the Company's common stock was established in connection with its IPO, the fair value of the Company's common stock was based on the IPO price per share and thereafter on its publicly traded common stock price at grant date, as listed on the Nasdaq Global Select Market under the ticker "ALMS."

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Valuation of Stock Options Granted under the 2024 POP

Stock options granted under the 2024 POP vest based on service, market and performance conditions (the occurrence of the IPO or a change of control) and are classified as equity financial instruments. At the grant date, the fair value of stock options granted under the 2024 POP was estimated using a Monte Carlo simulation model, which uses a distribution of potential outcomes on a monthly basis over the vesting period prioritizing the most reliable information available. The assumptions utilized in the calculation were based on the achievement of certain stock price thresholds, including the Company's expected common stock price, expected volatility, risk-free rate and expected term. The Company used the following assumptions to estimate the fair value at the grant date in May 2024: common stock fair value of \$12.06, vesting term of 6.0 years, volatility of 122.00%, and risk-free rate of 4.38%. The estimates of fair value are uncertain and changes in any of the estimated inputs could have resulted in significant adjustments to the fair value.

The Company's estimated fair value of stock options issued under the 2024 POP of \$18.0 million is recognized using graded vesting from July 1, 2024, the closing of the IPO, when the performance condition was met, over the longer of (i) the explicit service period of the service condition of 36 months or (ii) the derived service period between 1.4 years to 2.1 years), as determined for each graded vesting tranche. The Company recognized \$5.7 million in stock-based compensation expense related to the 2024 POP for the year ended December 31, 2024.

Early Exercise of Employee Stock Options

Proceeds from the early exercise of stock options are recorded as share repurchase liability, and as shares vest are recognized to additional paid-in capital in the consolidated balance sheets. As of December 31, 2024 and 2023, there was \$0.8 million and \$1.8 million share repurchase liability related to the unvested shares, respectively, included in share repurchase liability in the consolidated balance sheets.

The following table summarizes the activity for the Company's early exercisable shares for the years ended December 31, 2024 and 2023:

| | Number of Shares | Weighted- Average Exercise Price Per Share |
|----------------------------------|---------------------|---|
| Unvested as of December 31, 2022 | 663,930 | \$ 5.36 |
| Early exercised | 18,469 | \$ 9.48 |
| Vested | (340,502) | \$ 5.65 |
| Repurchased | (14,797) | \$ 4.36 |
| Unvested as of December 31, 2023 | 327,100 | \$ 5.33 |
| Early exercised | 25,034 | \$ 8.84 |
| Vested | (205,451) | \$ 5.62 |
| Unvested as of December 31, 2024 | <u>146,683</u> | \$ 5.53 |

Stock-Based Compensation Expense

The following table summarizes stock-based compensation expense recognized in the Company's consolidated statements of operations and comprehensive loss for the years ended December 31, 2024 and 2023 (in thousands):

| | Year Ended December 31, | |
|--|-------------------------|-----------------|
| | 2024 | 2023 |
| Research and development | \$ 10,110 | \$ 4,745 |
| General and administrative | 9,347 | 3,880 |
| Total stock-based compensation expense | <u>\$ 19,457</u> | <u>\$ 8,625</u> |

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The following table summarizes the stock-based compensation expense recognized in the Company's consolidated statements of operations and comprehensive loss by award type for the years ended December 31, 2024 and 2023 (in thousands):

| | Year Ended December 31, | |
|--|-------------------------|-----------------|
| | 2024 | 2023 |
| Stock options | \$ 19,399 | \$ 8,553 |
| Restricted stock awards | 58 | 72 |
| Total stock-based compensation expense | <u>\$ 19,457</u> | <u>\$ 8,625</u> |

Stock-based compensation expense related to non-employee awards was \$0.3 million for the years ended December 31, 2024 and 2023.

As of December 31, 2024, there was unrecognized stock-based compensation expense of \$54.4 million related to unvested stock options which the Company expects to recognize over a remaining weighted-average period of 2.5 years.

11. Net Loss Per Share Attributable to Common Stockholders

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders for the years ended December 31, 2024 and 2023 (in thousands, except share and per share amounts):

| | Year Ended December 31, | |
|---|-------------------------|-------------------|
| | 2024 | 2023 |
| Numerator: | | |
| Net loss | \$ (294,233) | \$ (154,993) |
| Denominator: | | |
| Weighted-average shares of common stock outstanding | 28,579,979 | 2,649,038 |
| Less: Weighted-average shares of common stock subject to repurchase | (238,113) | (498,852) |
| Weighted-average shares of common stock outstanding, basic and diluted | 28,341,866 | 2,150,186 |
| Net loss per share attributable to common stockholders, basic and diluted | <u>\$ (10.38)</u> | <u>\$ (72.08)</u> |

The following outstanding potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented, because including them would have been anti-dilutive (on an as-converted basis):

| | December 31, 2024 | December 31, 2023 |
|--|-------------------|-------------------|
| Stock options issued and outstanding | 9,458,788 | 5,096,086 |
| Unvested restricted common stock and early exercised stock options | 149,266 | 356,422 |
| Redeemable convertible preferred stock issued and outstanding | — | 18,387,168 |
| Total | <u>9,608,054</u> | <u>23,839,676</u> |

12. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2024 and 2023, as the Company operated with taxable losses. The Company has incurred net operating losses only in the United States since inception.

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The differences between the effective income tax rate and the U.S. federal statutory income tax rate for the years ended December 31, 2024 and 2023 were as follows (in thousands):

| | Year Ended December 31, | |
|---|-------------------------|-------------|
| | 2024 | 2023 |
| Amount at statutory tax rates | \$ (61,789) | \$ (32,548) |
| Permanent differences | 3,000 | 7 |
| Valuation allowance | 64,923 | 34,961 |
| Stock-based compensation | 3,356 | 892 |
| Federal research and development credit | (9,520) | (3,322) |
| Other | 30 | 10 |
| Total | \$ — | \$ — |

Significant components of the deferred tax asset balances as of December 31, 2024 and 2023 were as follows (in thousands):

| | December 31, 2024 | December 31, 2023 |
|---|----------------------|----------------------|
| Deferred tax assets: | | |
| Net operating losses | \$ 21,573 | \$ 10,519 |
| Tax credits | 17,407 | 6,243 |
| Research and development capitalization | 74,211 | 39,059 |
| Accruals and reserves | 115 | 15 |
| Stock-based compensation | 3,088 | 1,361 |
| Operating lease liabilities | 6,452 | 6,842 |
| Other capitalized expenses | 11,832 | 4,567 |
| Gross deferred tax assets | 134,678 | 68,606 |
| Valuation allowance | (127,990) | (61,404) |
| Deferred tax assets, net of valuation allowance | \$ 6,688 | \$ 7,202 |
| Deferred tax liabilities: | | |
| Fixed assets | (885) | (1,025) |
| Operating lease right-of-use assets | (5,803) | (6,177) |
| Deferred tax liabilities | (6,688) | (7,202) |
| Total net deferred tax assets | \$ — | \$ — |

A valuation allowance is required to be established when it is more likely than not that all or a portion of a deferred tax asset will not be realized. Realization of deferred tax assets is dependent upon future earnings, the timing and amount of which are uncertain. The Company believes that, based on a number of factors such as the history of operating losses, it is more likely than not that the deferred tax assets will not be fully realized, such that a full valuation allowance has been recorded. The valuation allowance increased by \$66.6 million and by \$35.4 million for the years ended December 31, 2024 and 2023, respectively, primarily due to the net operating losses carryforwards and research and development credits.

The following table sets forth the Company's U.S. federal and state net operating loss carryforwards and tax credits as of December 31, 2024 (in thousands):

| | Amount | Begin to Expire |
|------------------------------------|-----------|-----------------|
| Net operating losses, U.S. federal | \$ 84,664 | Do not expire |
| Net operating losses, U.S. federal | \$ 16,520 | 2037 |
| Net operating losses, U.S. states | \$ 4,683 | 2041 |
| Tax credits, U.S. federal | \$ 16,026 | 2039 |
| Tax credits, U.S. states | \$ 5,289 | 2037 |

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Utilization of some of the U.S. federal and state net operating loss and credit carryforwards may be subject to annual limitations due to the change in ownership provisions of the Internal Revenue Code and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. As of December 31, 2024, the Company has completed an Internal Revenue Code section 382 analysis which did not result in any expiration of U.S. federal net operating losses and credits before utilization. As the Company has recorded a full valuation allowance, any potential limitation is not expected to have a material impact to the consolidated financial statements.

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the unrecognized tax benefits for the years ended December 31, 2024 and 2023, is as follows (in thousands):

| | <u>Year Ended December 31,</u> | |
|--|--------------------------------|-----------------|
| | <u>2024</u> | <u>2023</u> |
| Beginning balance | \$ 4,116 | \$ 2,451 |
| Increases in tax positions in the current period | 1,336 | 3,572 |
| Decreases related to prior year's tax position | (2,655) | (1,907) |
| Ending balance | <u>\$ 2,797</u> | <u>\$ 4,116</u> |

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized. The Company has elected to include interest and penalties as a component of other income (expense), net. For the years ended December 31, 2024 and 2023, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly increase or decrease during the next 12 months.

As of December 31, 2024, the Company is not under audit by the Internal Revenue Service or any state authority for income taxes for any open years. Due to the Company's net operating loss carryforwards, the Company's domestic income tax returns are open to examination by the Internal Revenue Service beginning with tax year 2017 and by state taxing authorities beginning with tax year 2021.

13. Employee Benefit Plans

The Company sponsors a qualified 401(k) defined contribution plan covering eligible employees. Participants may contribute a portion of their annual compensation limited to a maximum annual amount set by the Internal Revenue Service. There were no employer contributions under this plan for the years ended December 31, 2024 and 2023.

14. Segment Reporting

For purposes of evaluating performance and allocating resources, the Company's CODM, its Chief Executive Officer, regularly reviews consolidated net loss as reported in the Company's consolidated statements of operations and comprehensive loss as compared to budget. The measure of segment assets is reported in the consolidated balance sheets as total consolidated assets.

ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

In addition to the significant expense categories included within consolidated net loss presented in the Company's consolidated statements of operations and comprehensive loss, see below for disaggregated amounts that comprise research and development expenses for the years ended December 31, 2024 and 2023 (in thousands):

| | Year Ended December 31, | |
|--|-------------------------|--------------|
| | 2024 | 2023 |
| Operating expenses: | | |
| Research and development expenses | | |
| External costs | | |
| Milestones related to previously acquired IPR&D assets | \$ 23,000 | \$ — |
| CRO, CMO and clinical trials | 151,422 | 68,967 |
| Professional consulting services | 19,154 | 13,155 |
| Other research and development costs | 10,258 | 11,463 |
| Internal costs | | |
| Personnel-related costs | 46,774 | 32,068 |
| Facilities and overhead costs | 14,946 | 12,023 |
| Total research and development expense | 265,554 | 137,676 |
| General and administrative expenses | 35,200 | 20,498 |
| Total operating expenses | 300,754 | 158,174 |
| Loss from operations | (300,754) | (158,174) |
| Total other income (expense), net | 6,521 | 3,181 |
| Consolidated net loss | \$ (294,233) | \$ (154,993) |

15. Subsequent Events

Merger Agreement

On February 6, 2025, the Company entered into an Agreement and Plan of Merger (the "Merger Agreement") with ACELYRIN, Inc., a Delaware corporation ("ACELYRIN"), and Arrow Merger Sub, Inc., a Delaware corporation and a direct wholly owned subsidiary of the Company ("Merger Sub"). Under the terms of the Merger Agreement, Merger Sub will merge with and into ACELYRIN, with ACELYRIN continuing as a direct wholly owned subsidiary of the Company (the "Merger"). The Merger Agreement was approved by the disinterested directors on the Company's board of directors and the board of directors of ACELYRIN and is subject to stockholder approval by the stockholders of each company and satisfaction or waiver of other closing conditions.

In connection with the Merger, all of the issued and outstanding shares of common stock of ACELYRIN, par value \$0.00001 per share (the "ACELYRIN Shares"), will be cancelled and converted into the right to receive 0.4274 shares of the Company's voting common stock, without interest (the number of shares of the Company's common stock in exchange for each ACELYRIN Share, the "Exchange Ratio") and, if applicable, cash in lieu of fractional shares, subject to any applicable withholding.

Consummation of the Merger is subject to certain closing conditions, including the absence of any law or judgment that restrains, enjoins or otherwise prohibits consummation of the Merger, the effectiveness of a registration statement on Form S-4 to be filed with the SEC by the Company, adoption of the Merger Agreement by the holders of a majority of the outstanding ACELYRIN Shares at ACELYRIN's stockholders' meeting, and approval of the share issuance by the holders of a majority of votes of the Company's common stock cast at the Company's stockholders' meeting.

The Merger Agreement contains certain termination rights for both the Company and ACELYRIN, including the right of either party to terminate the Merger Agreement if the transactions have not been consummated prior to July 7, 2025. The Company or ACELYRIN will pay a termination fee of \$10.0 million or \$10.0 million, respectively, under certain circumstances, including termination to accept and enter into a definitive agreement with respect to a superior proposal.

**ALUMIS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

Immediately following the Merger, the Company's pre-Merger equityholders are expected to collectively own approximately 55% of the shares of the combined company and the pre-Merger equityholders of ACELYRIN as of immediately prior to the Merger are expected to collectively own approximately 45% of the combined company, in each case, calculated on a fully diluted basis as of January 31, 2025.

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

None.

Item 9A. Controls and Procedures

Evaluation of the Effectiveness of Disclosure Controls and Procedures

As of December 31, 2024, management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of December 31, 2024, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the Company's registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the three months ended December 31, 2024, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on the Effectiveness of Controls

In designing and evaluating the disclosure controls and procedures, management recognizes that because of the inherent limitations in all control systems, any controls and procedures, no matter how well designed and operated, can provide only reasonable not absolute, assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and the benefits of controls and procedures must be considered relative to their costs.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and incorporated by reference to our definitive proxy statement for our 2025 annual meeting of stockholders (the “Proxy Statement”) to be filed pursuant Regulation 14A of the Exchange Act. If our Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is to be included in our Proxy Statement as follows and is incorporated by reference under the sections titled “Proposal 1: Election of Directors,” “Information Regarding the Board of Directors and Corporate Governance” and “Executive Officers,” provided that if the Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

We have adopted a Code of Business Conduct and Ethics that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the Code of Business Conduct and Ethics is available on the Corporate Governance section of our website at <https://investors.alumis.com/corporate-governance/documents-charters>. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director that are required to be disclosed pursuant to SEC rules, we will promptly disclose the nature of the amendment or waiver on our website or in a current report on Form 8-K.

We have adopted an insider trading policy applicable to its directors, officers and employees and other covered persons, governing the purchase, sale and other dispositions of our securities (the “Insider Trading Policy”). We believe that the Insider Trading Policy is reasonably designed to promote compliance with applicable U.S. insider trading laws, rules and regulations, and listing standards applicable to us. The Insider Trading Policy is filed as Exhibit 19.1 to this Annual Report on Form 10-K.

Item 11: Executive Compensation

The information required by this item is incorporated herein by reference to information contained in the Proxy Statement, including information within the section titled “Executive Compensation,” provided that if Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

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

The information required by this item is incorporated herein by reference to information contained in the Proxy Statement, including information within the sections titled, “Executive Compensation —Equity Compensation Plan Information” and “Security Ownership of Certain Beneficial Owners and Management,” provided that if Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

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

The information required by this item is incorporated herein by reference to information contained in the Proxy Statement, including information within the section titled, “Certain Relationships and Related Person Transactions” and “Information Regarding the Board of Directors and Corporate Governance—Director Independence,” provided that if Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated herein by reference to information contained in the Proxy Statement, including information within the section titled, “Proposal 2—Ratification of Selection of Independent Registered Public Accounting Firm,” provided that if Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)

- (1) Financial Statements – See the “*Index to Consolidated Financial Statements* included in Part II, Item 8. of this Annual Report on Form 10-K for a list of the financial statements filed as part of this report.
- (2) Financial Statement Schedules – All financial statement schedules have been omitted because the information required to be presented in them is not applicable or is shown in the consolidated financial statements or related notes, included in this Annual Report on Form 10-K.

b) Exhibits

| Exhibit Number | Description |
|----------------|---|
| 3.1 | Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant’s Current Report on Form 8-K, filed with the SEC on July 1, 2024) |
| 3.2 | Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant’s Current Report on Form 8-K, filed with the SEC on July 1, 2024) |
| 4.1 | Description of Capital Stock (incorporated by reference to the Registrant’s Registration Statement on Form 8-A (File No. 001-42143) filed with the SEC on June 25, 2024) |
| 4.2 | Amended and Restated Investors’ Rights Agreement, by and among the Registrant and certain of its stockholders, dated March 4, 2024 (incorporated by reference to Exhibit 4.2 to the Registrant’s Registration Statement on Form S-1 (file No. 333-280068), filed with the SEC on June 7, 2024) |
| 4.3* | Description of Capital Stock |
| 10.1 | Alumis Inc. 2021 Stock Plan, as amended (incorporated by reference to Exhibit 10.1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.2 | Forms of Stock Option Grant Notice under Alumis Inc. 2021 Stock Plan, as amended (incorporated by reference to Exhibit 10.2 to the Registrant’s Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.3 | Alumis Inc. 2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant’s Registration Statement on File Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |
| 10.4 | Forms of Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise under the Alumis Inc. 2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant’s Registration Statement on Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |
| 10.5 | Forms of Restricted Stock Unit Grant Notice and Award Agreement under the Alumis Inc. 2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant’s Registration Statement on Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |
| 10.6 | Alumis Inc. 2024 Performance Option Plan (incorporated by reference to Exhibit 10.6 to the Registrant’s Registration Statement on Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |
| 10.7 | Forms of Stock Option Grant Notice, Stock Options Agreement and Notice of Exercise under the Alumis Inc. 2024 Performance Option Plan (incorporated by reference to Exhibit 10.7 to the Registrant’s Registration Statement on Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |

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| 10.8 | Alumis Inc. 2024 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |
| 10.9* | Alumis Inc. Amended and Restated Non-Employee Director Compensation Policy |
| 10.10 | Form of Indemnification Agreement by and between Registrant and its directors and executive officers. (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1/A (File No. 333-280068), filed with the SEC on June 24, 2024) |
| 10.11 | Lease Agreement, dated as of August 11, 2022, by and between the Registrant and PG VII 280 East Grand, LLC (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.12 | Offer Letter, dated as of September 15, 2021, by and between the Registrant and Martin Babler (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.13 | Offer Letter, dated as of September 15, 2021, by and between the Registrant and David Goldstein (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.14 | Offer Letter, dated as of September 15, 2021, by and between the Registrant and Roy Hardiman (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.15 | Offer Letter, dated as of March 15, 2021, by and between the Registrant and Mark Bradley (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.16 | Amendment to Offer Letter, dated as of July 18, 2023, by and between the Registrant and Mark Bradley (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.17 | Offer Letter, dated as of November 12, 2021, by and between the Registrant and Derrick Richardson (incorporated by reference to Exhibit 10.18 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.18 | Offer Letter, dated as of January 12, 2022, by and between the Registrant and Sara Klein (incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.19 | Offer Letter, dated as of March 22, 2022, by and between the Registrant and John Schroer (incorporated by reference to Exhibit 10.20 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.20 | Offer Letter, dated as of June 24, 2022, by and between the Registrant and Jörn Drappa (incorporated by reference to Exhibit 10.21 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.21 | Stock Purchase Agreement, dated as of March 5, 2021, by and among the Registrant, FronThera International Group Limited and FronThera U.S. Holdings, Inc. (incorporated by reference to Exhibit 10.22 to the Registrant's Registration Statement on Form S-1 (File No. 333-280068), filed with the SEC on June 7, 2024) |
| 10.22 | Alumis Inc. Severance and Change in Control Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on February 21, 2025) |
| 19.1* | Alumis Inc. Insider Trading Policy |
| 23.1* | Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm of Alumis Inc. |

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|----------|--|
| 24.1* | Power of Attorney (included on signature page) |
| 31.1* | Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002 |
| 31.2* | Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002 |
| 32.1*# | Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 |
| 32.2*# | Certification of Chief 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* | Alumis Inc. Incentive Compensation Recoupment Policy |
| 101.INS* | XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document |
| 101.SCH* | XBRL Taxonomy Extension Schema Document |
| 101.CAL* | XBRL Taxonomy Extension Calculation Linkbase Document |
| 101.DEF* | XBRL Taxonomy Extension Definition Linkbase Document |
| 101.LAB* | XBRL Taxonomy Extension Label Linkbase Document |
| 101.PRE* | XBRL Taxonomy Extension Presentation Linkbase Document |
| 104* | Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101) |

* Filed herewith

This certification accompanies the Annual Report on Form 10-K pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and shall not be deemed to be “filed” by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Date: March 19, 2025

ALUMIS INC.

By: /s/ Martin Babler

Name: Martin Babler

Title: President and Chief Executive Officer

(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of Martin Babler and John Schroer his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below on March 19, 2025, by the following persons on behalf of the registrant and in the capacities indicated:

| <u>Signature</u> | <u>Title</u> |
|---|--|
| <u>/s/ Martin Babler</u> Martin Babler | President and Chief Executive Officer and Director <i>(Principal Executive Officer)</i> |
| <u>/s/ John Schroer</u> John Schroer | Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i> |
| <u>/s/ Srinivas Akkaraju, M.D., Ph.D.</u> Srinivas Akkaraju, M.D., Ph.D. | Director |
| <u>/s/ Alan B. Colowick, M.D., M.P.H.</u> Alan B. Colowick M.D., M.P.H. | Director |
| <u>/s/ Patrick Machado</u> Patrick Machado, J.D. | Director |
| <u>/s/ Sapna Srivastava, Ph.D.</u> Sapna Srivastava, Ph.D. | Director |
| <u>/s/ James B. Tananbaum, M.D.</u> James B. Tananbaum, M.D. | Director |
| <u>/s/ Zhengbin Yao, Ph.D.</u> Zhenbgin Yao, Ph.D. | Director |

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934**General**

Alumis Inc. has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our common stock, \$0.0001 par value per share. References herein to the terms the "company," "we," "our," and "us" refer to Alumis Inc.

The following description summarizes the most important terms of our capital stock and certain provisions of our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated investors' rights agreement, and relevant provisions of Delaware General Corporation Law ("DGCL"). The descriptions herein are summaries qualified in their entirety by our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated investors' rights agreement, copies of which have been incorporated by reference as exhibits to our Annual Report on Form 10-K, of which this Exhibit 4.1 is a part, as well as the relevant provisions of DGCL.

Our authorized capital stock consists of 492,815,092 shares of common stock, \$0.0001 par value per share, 7,184,908 shares of non-voting common stock, \$0.0001 par value per share, and 50,000,000 shares of preferred stock, \$0.0001 par value per share.

Common Stock and Non-Voting Common Stock***Voting Rights and Conversion Rights***

The holders of our common stock are entitled to one vote per share of common stock on any matter that is submitted to a vote of our stockholders, and holders of our non-voting common stock are not entitled to any votes per share of non-voting common stock, including for the election of directors. Additionally, holders of our common stock have no conversion rights, while holders of our non-voting common stock have the right to convert each share of our non-voting common stock into one share of common stock at such holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 4.99% of any class of our securities registered under the Exchange Act, unless otherwise as expressly provided for in our amended and restated certificate of incorporation. However, the beneficial ownership limitation may be increased to any other percentage designated by such holder of non-voting common stock upon 61 days' notice to us or decreased at any time. Holders of our non-voting common stock are also permitted to make certain transfers of non-voting common stock to non-affiliates upon which, such transferred shares could be immediately converted into shares of our common stock. Shares of our non-voting common stock are not otherwise subject to automatic or mandatory conversion for any reason.

Our amended and restated certificate of incorporation does not provide for cumulative voting for the election of directors for our common stock. Our amended and restated certificate of incorporation establishes a classified board of directors that is divided into three classes with staggered three-year terms. Only the directors in one class will be subject to election by a plurality of the votes cast at each annual meeting of our stockholders holding shares of common stock, with the directors in the other classes continuing for the remainder of their respective three-year terms. The affirmative vote of holders of at least 66 2/3% of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, is required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified structure of our board of directors, the size of our board of directors, removal of directors,

director liability, vacancies on our board of directors, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

Economic Rights

Except as otherwise expressly provided in our amended and restated certificate of incorporation or required by applicable law, and other than the voting rights and conversion rights stated above, all shares of common stock and non-voting common stock have the same rights and privileges and rank equally, share ratably, and are identical in all respects for all matters, including those described below.

Dividends. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock and non-voting common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Liquidation Rights. On our liquidation, dissolution, or winding-up, the holders of common stock and non-voting common stock will be entitled to share equally, identically, and ratably in all assets remaining after the payment of any liabilities, liquidation preferences and accrued or declared but unpaid dividends, if any, with respect to any outstanding preferred stock, unless a different treatment is approved by the affirmative vote of the holders of a majority of the outstanding shares of such affected class, voting separately as a class.

No Preemptive or Similar Rights

The holders of our shares of common stock and non-voting common stock are not entitled to preemptive rights, and are not subject to redemption or sinking fund provisions. The rights, preferences and privileges of the holders of our common stock or non-voting common stock are subject to, and may be adversely affected by, the right of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 50,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock and non-voting common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of our common stock and non-voting common stock and the voting and other rights of the holders of our common stock and non-voting common stock. We have no current plans to issue any shares of preferred stock.

Registration Rights

We are party to an amended and restated investors' rights agreement that provides certain holders of shares of our common stock, including certain holders of at least 5% of our capital stock and entities affiliated with certain of our directors, are entitled to certain rights with respect to registration of such

shares under the Securities Act of 1933, as amended (the “Securities Act”), as set forth below. These shares are referred to as registrable securities. This amended and restated investors’ rights agreement was entered into in March 2024. The registration of shares of our common stock (including shares of common stock issuable upon conversion of non-voting common stock) pursuant to the exercise of the registration rights described below would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions and limitations, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire no later than three years after the closing of our initial public offering.

Demand Registration Rights

The holders of the registrable securities are entitled to certain demand registration rights. The holders of 40% of these shares (or a lesser percent if the anticipated aggregate offering price, net of selling expenses, would exceed \$20.0 million) may request that we register all or a portion of their shares. We are not required to effect more than one registration statement which is declared or ordered effective.

Piggyback Registration Rights

The holders of the registrable securities are entitled to certain demand registration rights. In the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain piggyback registration rights allowing the holder to include their shares in such registration, subject to certain marketing and other limitations.

Form S-3 Registration Rights

The holders of the registrable securities are entitled to certain Form S-3 registration rights. Holders of 20% of these shares can make a request that we register their shares on Form S-3 if we are qualified to file a registration statement on Form S-3 and if the reasonably anticipated aggregate net proceeds of the shares offered would equal or exceed \$3.0 million. We will not be required to effect more than two registrations on Form S-3 within any 12-month period.

Anti-Takeover Provisions

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws, which are summarized below, may have the effect of delaying, deferring or discouraging another person from acquiring control of our company. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Certificate of Incorporation and Bylaws

Because our stockholders do not have cumulative voting rights, stockholders holding a majority of the voting power of our shares of common stock are able to elect all of our directors. Our amended and restated certificate of incorporation and our amended and restated bylaws provide for stockholder actions at a duly called meeting of stockholders or, before the date on which all shares of common stock convert into a single class, by written consent. A special meeting of stockholders may be called by a majority of our board of directors, the chair of our board of directors, or our chief executive officer or president. Our amended and restated bylaws include an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors.

In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes with staggered three-year terms.

The foregoing provisions make it more difficult for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of deterring hostile takeovers or delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, subject to certain exceptions.

Choice of Forum

Our amended and restated 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 and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) and any appellate court therefrom is the sole and exclusive forum for the following claims or causes of action under the Delaware statutory or common law: (i) any derivative claim or cause of action brought on our behalf; (ii) any claim or cause of action for a breach of fiduciary duty owed by any of our current or former directors, officers, or other employees to us or our stockholders; (iii) any claim or cause of action against us or any of our current or former directors, officers or other employees arising out of or pursuant to any provision of the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws (as each may be amended from time to time); (iv) any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws (as each may be amended from time to time, including any right,

obligation, or remedy thereunder); (v) any claim or cause of action as to which the DGCL confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any claim or cause of action against us or any of our current or former directors, officers, or other employees governed by the internal-affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants. Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States are the exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act, including all causes of action asserted against a defendant to such complaint. The choice of forum provision would not apply to claims or causes of action brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction.

For the avoidance of doubt, these provisions are intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. We note that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Additionally, our amended and restated certificate of incorporation provides that any person or entity holding, owning or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions.

Exchange Listing

Our common stock is listed on The Nasdaq Global Select Market under the symbol "ALMS." Our non-voting common stock is not listed on any securities exchange.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Equiniti Trust Company, LLC. The transfer agent's address is 48 Wall Street, Floor 23, New York, NY 10005.

ALUMIS INC.
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY
(AS AMENDED AND RESTATED ON FEBRUARY 7, 2025)

Each member of the Board of Directors (the “*Board*”) who is not also serving as an employee of or consultant to Alumis Inc. (the “*Company*”) or any of its subsidiaries (each such member, an “*Eligible Director*”) will receive the compensation described in this Non-Employee Director Compensation Policy for his or her Board service upon and following the date of the underwriting agreement between the Company and the underwriters managing the initial public offering of the Company’s common stock (the “*Common Stock*”), pursuant to which the Common Stock is priced in such initial public offering (the “*Effective Date*”). An Eligible Director may decline all or any portion of his or her compensation by giving notice to the Company prior to the date cash may be paid or equity awards are to be granted, as the case may be. This policy is effective as of the Effective Date and may be amended at any time in the sole discretion of the Board or the Compensation Committee of the Board.

Annual Cash Compensation

The annual cash compensation amount set forth below is payable to Eligible Directors in equal quarterly installments, payable in arrears on the last day of each fiscal quarter in which the service occurred. If an Eligible Director joins the Board or a committee of the Board at a time other than effective as of the first day of a fiscal quarter, each annual retainer set forth below will be pro-rated based on days served in the applicable fiscal quarter, with the pro-rated amount paid on the last day of the first fiscal quarter in which the Eligible Director provides the service and regular full quarterly payments thereafter. All annual cash fees are vested upon payment.

1. Annual Board Service Retainer:
 - a. All Eligible Directors: \$40,000
 - b. Non-Executive Chair of the Board Service Retainer (in addition to Eligible Director Service Retainer): \$30,000

2. Annual Committee Chair Service Retainer:
 - a. Chair of the Audit Committee: \$20,000
 - b. Chair of the Compensation Committee: \$15,000
 - c. Chair of the Nominating and Corporate Governance Committee: \$10,000

3. Annual Committee Member Service Retainer (not applicable to Committee Chairs):
 - a. Member of the Audit Committee: \$10,000
 - b. Member of the Compensation Committee: \$7,500
 - c. Member of the Nominating and Corporate Governance Committee: \$5,000

Expenses

The Company will reimburse Eligible Directors for ordinary, necessary and reasonable out-of-pocket travel expenses to cover in-person attendance at and participation in Board and committee meetings; provided, that the Eligible Director timely submit to the Company appropriate

documentation substantiating such expenses in accordance with the Company's travel and expense policy, as in effect from time to time.

Equity Compensation

The equity compensation set forth below will be granted under the Company's 2024 Equity Incentive Plan (the "**Plan**"), subject to the approval of the Plan by the Company's stockholders. All stock options granted under this policy will be nonstatutory stock options, with an exercise price per share equal to 100% of the Fair Market Value (as defined in the Plan) of the underlying Common Stock on the date of grant, and a term of ten years from the date of grant (subject to earlier termination in connection with a termination of service as provided in the Plan).

1. **Initial Grants:** For each Eligible Director who is first elected or appointed to the Board following the Effective Date, on the date of such Eligible Director's initial election or appointment to the Board (or, if such date is not a market trading day, the first market trading day thereafter), the Eligible Director will automatically, and without further action by the Board or the Compensation Committee of the Board, be granted a stock option to purchase 52,000 shares of Common Stock (the "**Initial Grant**"). The shares subject to each Initial Grant will vest over a three-year period, with 1/36th of the shares subject to the Initial Grant vesting in equal monthly installments following the date of grant, such that the option is fully vested on the third anniversary of the date of grant, subject to the Eligible Director's Continuous Service (as defined in the Plan) through each such vesting date, and will vest in full upon a Change in Control (as defined in the Plan), subject to the Eligible Director's Continuous Service through such date.

2. **Annual Grants:** On the date of each annual stockholder meeting of the Company held after the Effective Date, each Eligible Director who continues to serve as a non-employee member of the Board following such stockholder meeting (excluding any Eligible Director who is first appointed or elected by the Board at such meeting) will automatically, and without further action by the Board or the Compensation Committee of the Board, be granted a stock option to purchase 26,000 shares of Common Stock (the "**Annual Grant**"). The shares subject to the Annual Grant will vest in full on the first anniversary of the date of grant, subject to the Eligible Director's Continuous Service through such vesting date; provided, that the Annual Grant will in any case be fully vested on the date of Company's next annual stockholder meeting, subject to the Eligible Director's Continuous Service through such vesting date; provided, further, that the Annual Grant will vest in full upon a Change in Control, subject to the Eligible Director's Continuous Service through such date. With respect to an Eligible Director who, following the Effective Date, was first elected or appointed to the Board on a date other than the date of the Company's annual stockholder meeting, upon the Company's first annual stockholder meeting following such Eligible Director's first joining the Board, such Eligible Director's first Annual Grant will be pro-rated to reflect the time between such Eligible Director's election or appointment date and the date of such first annual stockholder meeting.

Non-Employee Director Compensation Limit

Notwithstanding the foregoing, the aggregate value of all compensation granted or paid, as applicable, to any individual for service as a Non-Employee Director (as defined in the Plan) shall in no event exceed the limits set forth in Section 3(d) of the Plan.

ALUMIS INC.
INSIDER TRADING POLICY

(AS AMENDED DECEMBER 6, 2024)

INTRODUCTION

During the course of your relationship with Alumis Inc. (“*Alumis*”), you may receive material information that is not yet publicly available (“*material nonpublic information*”) about Alumis or other publicly traded companies that Alumis has business relationships with. Material nonpublic information may give you, or someone you pass that information on to, a leg up over others when deciding whether to buy, sell or otherwise transact in Alumis’ securities or the securities of another publicly traded company. This policy sets forth guidelines with respect to transactions in Alumis securities by our employees, directors and consultants who are advised that they are subject to this policy (“*designated consultants*”) and the other persons subject to this policy as described below.

STATEMENT OF POLICY

It is the policy of Alumis that an employee, director or designated consultant of Alumis (or any other person subject to this policy) who is aware of material nonpublic information relating to Alumis **may not**, directly or indirectly:

1. engage in any transactions in Alumis’ securities, except as otherwise specified under the heading “Exceptions to this Policy” below;
2. recommend the purchase or sale of any Alumis’ securities;
3. disclose material nonpublic information to persons within Alumis whose jobs do not require them to have that information, or outside of Alumis to other persons, such as family, friends, business associates and investors, unless the disclosure is made in accordance with Alumis’ policies regarding the protection or authorized external disclosure of information regarding Alumis; or
4. assist anyone engaged in the above activities.

The prohibition against insider trading is absolute. It applies *even if* the decision to trade is not based on such material nonpublic information. It also applies to transactions that may be necessary or justifiable for independent reasons (such as the need to raise money for an emergency expenditure) and also to very small transactions. All that matters is whether you are aware of **any** material nonpublic information relating to Alumis at the time of the transaction.

The U.S. federal securities laws do not recognize any mitigating circumstances to insider trading. In addition, even the appearance of an improper transaction must be avoided to preserve Alumis’ reputation for adhering to the highest standards of conduct. In some circumstances, you may need to forgo a planned transaction even if you planned it before becoming aware of the material nonpublic information. So, even if you believe you may suffer an economic loss or sacrifice an anticipated profit by waiting to trade, you must wait.

It is also important to note that the laws prohibiting insider trading are not limited to trading by the insider alone; advising others to trade on the basis of material nonpublic information is illegal and squarely prohibited by this policy. Liability in such cases can extend both to the “tippee”—the person to whom the

insider disclosed material nonpublic information—and to the “tipper,” the insider himself or herself. In such cases, you can be held liable for your own transactions, as well as the transactions by a tippee and even the transactions of a tippee’s tippee. For these and other reasons, it is the policy of Alumis that no employee, director or designated consultant of Alumis (or any other person subject to this policy) may either (a) recommend to another person that they buy, hold or sell Alumis’ securities **at any time** or (b) disclose material nonpublic information to persons within Alumis whose jobs do not require them to have that information, or outside of Alumis to other persons (unless the disclosure is made in accordance with Alumis’ policies regarding the protection or authorized external disclosure of information regarding Alumis).

In addition, it is the policy of Alumis that no employee, director or designated consultant of Alumis (or any other person subject to this policy) who, in the course of working for Alumis, learns of or is otherwise aware of material nonpublic information about another publicly traded company with which Alumis does business, including a partner or collaborator of Alumis, may trade in that company’s securities until the information becomes public or is no longer material.

There are no exceptions to this policy, except as specifically noted.

TRANSACTIONS SUBJECT TO THIS POLICY

This policy applies to all transactions in securities issued by Alumis, as well as derivative securities that are not issued by Alumis, such as exchange-traded put or call options or swaps relating to Alumis’ securities. Accordingly, for purposes of this policy, the terms “*trade*,” “*trading*” and “*transactions*” include not only purchases and sales of Alumis’ common stock in the public market but also any other purchases, sales, transfers or other acquisitions and dispositions of common or preferred equity, options, warrants and other securities (including debt securities) and other arrangements or transactions that affect economic exposure to changes in the prices of these securities.

PERSONS SUBJECT TO THIS POLICY

This policy applies to you and all other employees, directors and designated consultants of Alumis and its subsidiaries. This policy also applies to members of your immediate family, persons with whom you share a household, persons who are your economic dependents and any other individuals or entities whose transactions in securities you influence, direct or control (including, e.g., a venture or other investment fund, if you influence, direct or control transactions by the fund). The foregoing persons who are deemed subject to this policy are referred to in this policy as “*Related Persons*.” You are responsible for making sure that your Related Persons comply with this policy.

MATERIAL NONPUBLIC INFORMATION

Material information

It is not always easy to figure out whether you are aware of material nonpublic information. But there is one important factor to determine whether nonpublic information you know about a public company is material: whether the information could be expected to affect the market price of that company’s securities or to be considered important by investors who are considering trading that company’s securities. If the information makes you want to trade, it would probably have the same effect on others. Keep in mind that both positive and negative information can be material.

There is no bright-line standard for assessing materiality; rather, materiality is based on an assessment of all of the facts and circumstances, and is often evaluated by relevant enforcement authorities with the

benefit of hindsight. Depending on the specific details, the following items may be considered material nonpublic information until publicly disclosed within the meaning of this policy. There may be other types of information that would qualify as material information as well; use this list merely as a non-exhaustive guide:

- financial results or forecasts;
- status of product or product candidate development or regulatory approvals;
- clinical or pre-clinical data relating to products or product candidates;
- timelines for pre-clinical studies or clinical trials;
- acquisitions or dispositions of assets, divisions or companies;
- public or private sales of debt or equity securities;
- stock splits, dividends or changes in dividend policy;
- the establishment of a repurchase program for Alumis' securities;
- gain or loss of a significant licensor, licensee or supplier; and
- changes to or new corporate partner relationships or collaborations.
- notice of issuance or denial of patents;
- regulatory developments;
- management or control changes;
- employee layoffs;
- a disruption to or a delay in manufacturing of Alumis' products or product candidates;
- a disruption in Alumis' operations or breach or unauthorized access of its property or assets, including its facilities and information technology infrastructure;
- tender offers or proxy fights;
- accounting restatements;
- litigation or settlements; and
- impending bankruptcy.

When information is considered public

The prohibition on trading when you have material nonpublic information lifts once that information becomes publicly disseminated. But for information to be considered publicly disseminated, it must be widely disseminated through a press release, a filing with the Securities and Exchange Commission (the "**SEC**"), or other widely disseminated announcement. Once information is publicly disseminated, it is still necessary to afford the investing public with sufficient time to absorb the information. Generally speaking, information will be considered publicly disseminated for purposes of this policy **only after two full trading days have elapsed since the information was publicly disclosed**. For example, if we announce material nonpublic information before trading begins on Wednesday, then you may execute a transaction in our securities on Friday; if we announce material nonpublic information after trading ends on Wednesday, then you may execute a transaction in our securities on Monday. Depending on the particular circumstances, Alumis may determine that a longer waiting period should apply to the release of specific material nonpublic information.

QUARTERLY TRADING BLACKOUTS (NOT YET IMPLEMENTED)

Note: As a company still engaged in clinical development and without approved products for sale or earnings, Alumis is not currently implementing quarterly trading blackouts. However, Alumis may choose to commence quarterly trading blackouts at any time, and will inform employees in advance of implementing quarterly trading blackouts, in which case the following policy will apply.

Because our workplace culture tends to be open, odds are that the vast majority of our employees, directors and designated consultants will possess material nonpublic information at certain points during the year. To minimize even the appearance of insider trading among our employees, directors and designated consultants we have established “quarterly trading blackout periods” during which Alumis employees, directors, designated consultants and their Related Persons—regardless of whether they are aware of material nonpublic information or not—may not conduct any trades in Alumis securities. That means that, except as described in this policy, all Alumis employees, directors, designated consultants and their Related Persons will be able to trade in Alumis securities only during limited open trading window periods that generally will begin after two full trading days have elapsed since the public dissemination of Alumis’ annual or quarterly financial results and end at the beginning of the next quarterly trading blackout period (as defined below). Of course, even during an open trading window period, you may not (unless an exception applies) conduct any trades in Alumis securities if you are otherwise in possession of material nonpublic information.

For purposes of this policy, each “*quarterly trading blackout period*” will generally begin at the end of the day that is three weeks before the end of each fiscal quarter and end after two full trading days have elapsed since the public dissemination of Alumis’ financial results for that quarter. Please note that the quarterly trading blackout period may commence early or may be extended if, in the judgment of the Chief Executive Officer, Chief Financial Officer or Chief Legal Officer, there exists undisclosed information that would make trades by Alumis employees, directors and designated consultants inappropriate. It is important to note that the fact that the quarterly trading blackout period has commenced early or has been extended should be considered material nonpublic information that should not be communicated to any other person.

An Alumis employee, director or designated consultant who believes that special circumstances require him or her to trade during a quarterly trading blackout period should consult the Chief Legal Officer. Permission to trade during a quarterly trading blackout period will be granted only where the circumstances are extenuating, the Chief Legal Officer concludes that the person is not in fact aware of any material nonpublic information relating to Alumis or its securities, and there appears to be no significant risk that the trade may subsequently be questioned.

EVENT-SPECIFIC TRADING BLACKOUTS

From time to time, an event may occur that is material to Alumis and is known by only a few directors, officers and/or employees. So long as the event remains material and nonpublic, the persons designated by the Chief Executive Officer, Chief Financial Officer or Chief Legal Officer may not trade in Alumis’ securities. In that situation, Alumis will notify the designated individuals that neither they nor their Related Persons may trade in the Alumis’ securities. The existence of an event-specific trading blackout should also be considered material nonpublic information and should not be communicated to any other person. Even if you have not been designated as a person who should not trade due to an event-specific trading blackout, you are not allowed to trade while aware of material nonpublic information. Exceptions will not be granted during an event-specific trading blackout.

The quarterly and event-driven trading blackouts do not apply to those transactions to which this policy does not apply, as described under the heading “Exceptions to this Policy” below.

EXCEPTIONS TO THIS POLICY

This policy does not apply in the case of the following transactions, except as specifically noted:

1. **Option Exercises.** This policy **does not apply** to the exercise of options granted under Alumis’ equity compensation plans for cash or, where permitted under the option, by a net exercise transaction with

the Company or by delivery to Alumis of already-owned Alumis stock. This policy **does apply**, however, to any sale of stock as part of a broker-assisted cashless exercise or any other market sale, whether or not for the purpose of generating the cash needed to pay the exercise price or pay taxes.

2. **Tax Withholding Transactions.** This policy does not apply to the surrender of shares directly to Alumis to satisfy tax withholding obligations as a result of the issuance of shares upon vesting or exercise of restricted stock units, options or other equity awards granted under Alumis' equity compensation plans. Of course, any market sale of the stock received upon exercise or vesting of any such equity awards remains subject to all provisions of this policy whether or not for the purpose of generating the cash needed to pay the exercise price or pay taxes.

3. **ESPP.** This policy does not apply to the purchase of stock by employees under Alumis' Employee Stock Purchase Plan ("**ESPP**") on periodic designated dates in accordance with the ESPP. This policy does, however, apply to any sale of stock acquired pursuant to the ESPP.

4. **10b5-1 Automatic Trading Programs.** Under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended ("**Exchange Act**"), and as permitted by Alumis, employees, directors and consultants may establish a trading plan under which a broker is instructed to buy and sell Alumis securities based on pre-determined criteria (a "**Trading Plan**"). So long as a Trading Plan is properly established, purchases and sales of Alumis securities pursuant to that Trading Plan are not subject to this policy. To be properly established, an employee's, director's or consultant's Trading Plan must be established in compliance with the requirements of Rule 10b5-1 of the Exchange Act and Alumis' 10b5-1 Trading Plan Guidelines at a time when they were unaware of any material nonpublic information relating to Alumis and when Alumis was not otherwise in a trading blackout period. Moreover, all Trading Plans must be reviewed and approved by Alumis before being established to confirm that the Trading Plan complies with all pertinent company policies and applicable securities laws.

5. **Gifts.** This policy does not apply to *bona fide* charitable gifts of Alumis securities that have been pre-cleared by Alumis' Chief Legal Officer, Chief Financial Officer or his or her designee. Whether a gift is truly *bona fide* will depend on the facts and circumstances surrounding each gift. Pre-clearance is recommended to be sought at least two business days in advance of the proposed gift, and pre-cleared gifts not completed within five business days will require new pre-clearance. Alumis may choose to shorten this period.

SPECIAL AND PROHIBITED TRANSACTIONS

1. **Inherently Speculative Transactions.** No Alumis employee, director or designated consultant may engage in short sales, transactions in put options, call options or other derivative securities on an exchange or in any other organized market, or in any other inherently speculative transactions with respect to Alumis' stock.

2. **Hedging Transactions.** Hedging or monetization transactions can be accomplished through a number of possible mechanisms, including through the use of financial instruments such as prepaid variable forwards, equity swaps, collars and exchange funds. Such hedging transactions may permit an Alumis employee, director or designated consultant to continue to own Alumis' securities obtained through employee benefit plans or otherwise, but without the full risks and rewards of ownership. When that occurs, the Alumis employee, director or designated consultant may no longer have the same objectives as Alumis' other shareholders. Therefore, Alumis employees, directors and designated consultants are prohibited from engaging in any such transactions.

3. **Margin Accounts and Pledged Securities.** Securities held in a margin account as collateral for a margin loan may be sold by the broker without the customer's consent if the customer fails to meet a margin call. Similarly, securities pledged (or hypothecated) as collateral for a loan may be sold in foreclosure if the borrower defaults on the loan. Because a margin sale or foreclosure sale may occur at a time when the pledgor is aware of material nonpublic information or otherwise is not permitted to trade in Alumis' securities, Alumis employee, director and designated consultants are prohibited to use Alumis' securities as collateral for a loan.

4. **Standing and Limit Orders.** Standing and limit orders (except standing and limit orders under approved Trading Plans, as discussed above) create heightened risks for insider trading violations similar to the use of margin accounts. There is no control over the timing of purchases or sales that result from standing instructions to a broker, and as a result the broker could execute a transaction when an Alumis employee, director or designated consultant is in possession of material nonpublic information. Alumis therefore strongly discourages placing standing or limit orders on Alumis' securities. If a person subject to this policy determines that they must use a standing order or limit order (other than under an approved Trading Plan as discussed above), the order should be limited to short duration and the person using such standing order or limit order is required to cancel such instructions immediately in the event restrictions are imposed on their ability to trade pursuant to the "Quarterly Trading Blackouts" and "Event-Specific Trading Blackouts" provisions above.

PRE-CLEARANCE AND ADVANCE NOTICE OF TRANSACTIONS

For purposes of this policy, Alumis' board of directors has designated the Chief Legal Officer of the Company as the Clearing Officer, who has the authority to delegate, in writing, such preclearance duties to other attorney(s) within the Legal Department as an Alternate Clearing Officer (all together hereafter referred to as Clearing Officers). In addition to the requirements above, employees, officers, directors and other applicable members of management who have been notified that they are subject to pre-clearance requirements (which will be all employees until further notice) face a further restriction: Even during an open trading window, they may not engage in any transaction in Alumis' securities without first obtaining pre-clearance of the transaction from the Clearing Officers or designee, recommended to be sought at least two business days in advance of the proposed transaction. The Clearing Officers or designee will then determine whether the transaction may proceed and, if so, will direct the Compliance Officer (our Chief Legal Officer) to help comply with any required reporting requirements under Section 16(a) of the Exchange Act. Pre-cleared transactions not completed within five business days will require new pre-clearance. Alumis may choose to shorten this period.

Section 16 officers and directors must also give advance notice of their plans to exercise an outstanding stock option to a Clearing Officer. Once any transaction takes place, the officer, director or applicable member of management must immediately notify the Clearing Officer so that Alumis may assist in any Section 16 reporting obligations.

SHORT-SWING TRADING, CONTROL STOCK AND SECTION 16 REPORTS

Officers and directors subject to the reporting obligations under Section 16 of the Exchange Act should take care to avoid short-swing transactions (within the meaning of Section 16(b) of the Exchange Act) and the restrictions on sales by control persons (Rule 144 under the Securities Act of 1933, as amended), and should file all appropriate Section 16(a) reports (Forms 3, 4 and 5), which are described in Alumis' Section 16 Compliance Program, and any notices of sale required by Rule 144.

POLICY'S DURATION

This policy continues to apply to your transactions in Alumis' securities or the securities of other public companies engaged in business transactions with Alumis even after your relationship with Alumis has ended. If you are aware of material nonpublic information when your relationship with Alumis ends, you may not trade Alumis' securities or the securities of other applicable companies until the material nonpublic information has been publicly disseminated or is no longer material. Further, if you leave Alumis during a trading blackout period, then you may not trade Alumis' securities or the securities of other applicable companies until the trading blackout period has ended.

INDIVIDUAL RESPONSIBILITY

Persons subject to this policy have ethical and legal obligations to maintain the confidentiality of information about Alumis and to not engage in transactions in Alumis' securities while aware of material nonpublic information. Each individual is responsible for making sure that he or she complies with this policy, and that any family member, household member or other person or entity whose transactions are subject to this policy, as discussed under the heading "Persons Subject to this Policy" above, also comply with this policy. In all cases, the responsibility for determining whether an individual is aware of material nonpublic information rests with that individual, and any action on the part of Alumis or any employee or director of Alumis pursuant to this policy (or otherwise) does not in any way constitute legal advice or insulate an individual from liability under applicable securities laws. You could be subject to severe legal penalties and disciplinary action by Alumis for any conduct prohibited by this policy or applicable securities laws. See "Penalties" below.

PENALTIES

Anyone who engages in insider trading or otherwise violates this policy may be subject to both civil liability and criminal penalties. Violators also risk disciplinary action by Alumis, including termination of employment. Anyone who has questions about this policy should contact their own attorney or Alumis' legal department. Please also see Frequently Asked Questions, which are attached as **EXHIBIT A**.

AMENDMENTS

Alumis is committed to continuously reviewing and updating its policies and procedures. Alumis therefore reserves the right to amend, alter or terminate this policy at any time and for any reason. A current copy of Alumis' policies regarding insider trading may be obtained by going to Alumis Pulse for policies.

EXHIBIT A
INSIDER TRADING POLICY
FREQUENTLY ASKED QUESTIONS

1. *What is insider trading?*

A: Generally speaking, insider trading is the buying or selling of stocks, bonds, futures or other securities by someone who possesses or is otherwise aware of material nonpublic information about the securities or the issuer of the securities. Insider trading also includes trading in derivatives (such as put or call options) where the price is linked to the underlying price of a company's stock. It does not matter whether the decision to buy or sell was influenced by the material nonpublic information, how many shares you buy or sell, or whether it has an effect on the stock price. Bottom line: If you are aware of material nonpublic information about Alumis or another publicly traded company that Alumis has business relationships with and you trade in Alumis' or such other company's securities, you have broken the law.

2. *Why is insider trading illegal?*

A: If company insiders are able to use their confidential knowledge to their financial advantage, other investors would not have confidence in the fairness and integrity of the market. This ensures that there is an even playing field by requiring those who are aware of material nonpublic information to refrain from trading.

3. *What is material nonpublic information?*

A: Information is material if it would influence a reasonable investor to buy or sell a stock, bond future or other security. This could mean many things: financial results, clinical or regulatory results, potential acquisitions or major contracts to name just a few. Information is nonpublic if it has not yet been publicly disseminated within the meaning of our insider trading policy.

4. *Who can be guilty of insider trading?*

A: Anyone who buys or sells a security while aware of material nonpublic information, or provides material nonpublic information that someone else uses to buy or sell a security, may be guilty of insider trading. This applies to all individuals, including officers, directors and others who don't even work at Alumis. Regardless of who you are, if you know something material about the value of a security that not everyone knows and you trade (or convince someone else to trade) in that security, you may be found guilty of insider trading.

5. *Does Alumis have an insider trading policy?*

A: Yes, please see the insider trading policy that these Frequently Asked Questions are appended to.

6. *What if I don't buy or sell anything, but I tell someone else material nonpublic information and they buy or sell?*

A: That is called "tipping." You are the "tipper" and the other person is called the "tippee." If the tippee buys or sells based on that material nonpublic information, both you and the "tippee" could be found guilty of insider trading. In fact, if you tell family members who tell others and those people then trade on the information, those family members and the "tippee" might be found guilty of insider trading too. To prevent this, you may not discuss material nonpublic information about the company with anyone outside

Alumis, including spouses, family members, friends or business associates (unless the disclosure is made in accordance with Alumis' policies regarding the protection or authorized external disclosure of information regarding Alumis). This includes anonymous discussions on the internet about Alumis or companies with which Alumis does business.

7. *What if I don't tell them the information itself; I just tell them whether they should buy or sell?*

A: That is still tipping, and you can still be responsible for insider trading. You may never recommend to another person that they buy, hold or sell Alumis' common stock or any derivative security related to Alumis' common stock, since that could be a form of tipping.

8. *What are the sanctions if I trade on material nonpublic information or tip off someone else?*

A: In addition to disciplinary action by Alumis—which may include termination of employment—you may be liable for civil sanctions for trading on material nonpublic information. The sanctions may include return of any profit made or loss avoided as well as penalties of up to three times any profit made or any loss avoided. Persons found liable for tipping material nonpublic information, even if they did not trade themselves, may be liable for the amount of any profit gained or loss avoided by everyone in the chain of tippees as well as a penalty of up to three times that amount. In addition, anyone convicted of criminal insider trading could face prison and additional fines.

9. *What is "loss avoided"?*

A: If you sell common stock or a related derivative security before negative news is publicly announced, and as a result of the announcement the stock price declines, you have avoided the loss caused by the negative news.

10. *Am I restricted from trading securities of any companies other than Alumis, for example a partner or competitor of Alumis?*

A: Possibly. U.S. insider trading laws generally restrict everyone aware of material nonpublic information about a company from trading in that company's securities, regardless of whether the person is directly connected with that company, except in limited circumstances. Therefore, if you have material nonpublic information about another company, you should not trade in that company's securities. You should be particularly conscious of this restriction if, through your position at Alumis, you sometimes obtain sensitive, material information about other companies and their business dealings with Alumis.

11. *So if I do not trade Alumis securities when I have material nonpublic information, and I don't "tip" other people, I am in the clear, right?*

A: Not necessarily. Even if you do not violate U.S. law, you may still violate our policies. For example, employees and consultants may violate our policies by breaching their confidentiality obligations or by recommending Alumis stock as an investment, even if these actions do not violate securities laws. Our policies are stricter than the law requires so that we and our employees and consultants can avoid even the appearance of wrongdoing. Therefore, please review the entire policy carefully.

12. *So when can I buy or sell my Alumis securities?*

A: If you are aware of material nonpublic information, you may not buy or sell our common stock until two full trading days have elapsed since the information was publicly disclosed. At that point, the information is considered publicly disseminated for purposes of our insider trading policy. For example, if

we announce material nonpublic information before trading begins on Wednesday, then you may execute a transaction in our securities on Friday; if we announce material nonpublic information after trading ends on Wednesday, then you may execute a transaction in our securities on Monday. **Even if you are not aware of any material nonpublic information, you may not trade our common stock during any trading “blackout” period.** Our insider trading policy describes the quarterly trading blackout period, and additional event-driven trading blackout periods may be announced by email.

13. *If I have an open order to buy or sell Alumis securities on the date a blackout period commences, can I leave it to my broker to cancel the open order and avoid executing the trade?*

A: No, unless it is in connection with a 10b5-1 trading plan (see Question 26 below). If you have any open orders when a blackout period commences other than in connection with a 10b5-1 trading plan, it is your responsibility to cancel these orders with your broker. If you have an open order and it executes after a blackout period commences not in connection with a 10b5-1 trading plan, you will have violated our insider trading policy and may also have violated insider trading laws.

14. *Am I allowed to trade derivative securities of Alumis’ common stock?*

A: No. Under our policies, you may not trade in derivative securities related to our common stock, which include publicly traded call and put options. In addition, under our policies, you may not engage in short selling of our common stock at any time.

“Derivative securities” are securities other than common stock that are speculative in nature because they permit a person to leverage their investment using a relatively small amount of money. Examples of derivative securities include “put options” and “call options.” These are different from employee options and other equity awards granted under our equity compensation plans, which are not derivative securities for purposes of our policy.

“Short selling” is profiting when you expect the price of the stock to decline, and includes transactions in which you borrow stock from a broker, sell it, and eventually buy it back on the market to return the borrowed shares to the broker. Profit is realized if the stock price decreases during the period of borrowing.

15. *Why does Alumis prohibit trading in derivative securities and short selling?*

A: Many companies with volatile stock prices have adopted similar policies because of the temptation it represents to try to benefit from a relatively low-cost method of trading on short-term swings in stock prices, without actually holding the underlying common stock, and encourages speculative trading. We are dedicated to building stockholder value, short selling our common stock conflicts with our values and would not be well-received by our stockholders.

16. *Can I purchase Alumis securities on margin or hold them in a margin account?*

A: No. Under our policies, you may not purchase our common stock on margin or hold it in a margin account at any time.

“Purchasing on margin” is the use of borrowed money from a brokerage firm to purchase our securities. Holding our securities in a margin account includes holding the securities in an account in which the shares can be sold to pay a loan to the brokerage firm.

17. Why does Alumis prohibit me from purchasing Alumis securities on margin or holding them in a margin account?

A: Margin loans are subject to a margin call whether or not you possess material nonpublic information at the time of the call. If a margin call were to be made at a time when you were aware of material nonpublic information and you could not or did not supply other collateral, you may be liable under insider trading laws because of the sale of the securities (through the margin call). The sale would be attributed to you even though the lender made the ultimate determination to sell. The U.S. Securities and Exchange Commission takes the view that you made the determination to not supply the additional collateral and you are therefore responsible for the sale.

18. Can I pledge my Alumis shares as collateral for a personal loan?

A: No. Pledging your shares as collateral for a personal loan could cause the pledgee to transfer your shares during a trading blackout period or when you are otherwise aware of material nonpublic information. As a result, you may not pledge your shares as collateral for a loan.

19. Can I hedge my ownership position in Alumis?

A: Hedging or monetization transactions, including through the use of financial instruments such as prepaid variable forwards, equity swaps, collars and exchange funds are prohibited by our insider trading policy. Since such hedging transactions allow you to continue to own Alumis' securities obtained through employee benefit plans or otherwise, but without the full risks and rewards of ownership, you may no longer have the same objectives as Alumis' other shareholders. Therefore, our insider trading policy prohibits you from engaging in any such transactions.

20. Can I exercise options granted to me under Alumis' equity compensation plans during a trading blackout period or when I possess material nonpublic information?

A: It depends. You **may exercise** the options for cash (or via net exercise transaction with the company) and receive shares, **but you may not** sell the shares (even to pay the exercise price or any taxes due) during a trading blackout period or any time that you are aware of material nonpublic information. To be clear, you may not effect a broker-assisted cashless exercise (these cashless exercise transactions include a market sale) during a trading blackout period or any time that you are aware of material nonpublic information

21. Am I subject to trading blackout periods if I am no longer an employee or consultant of Alumis?

A: It depends. If your employment with Alumis ends during a trading blackout period, you will be subject to the remainder of that trading blackout period. If your employment with Alumis ends on a day that the trading window is open, you will not be subject to the next trading blackout period. However, even if you are not subject to our trading blackout period after you leave Alumis, you should not trade in Alumis securities if you are aware of material nonpublic information. That restriction stays with you as long as the information you possess is material and not publicly disseminated within the meaning of our insider trading policy.

22. Can I gift stock while I possess material nonpublic information or during a trading blackout period?

A: It depends. Because of the potential for the appearance of impropriety, you may only make *bona fide* gifts of our common stock when you are aware of material nonpublic information or during a

trading blackout period if (and only if) the gift has been pre-cleared by Alumis' Chief Legal Officer, Chief Financial Officer or his or her designee. Whether a gift is truly *bona fide* will depend on the facts and circumstances surrounding each gift.

23. *What if I purchased publicly traded options or other derivative securities before I became an Alumis employee or consultant?*

A: The same rules apply as for employee stock options. You may exercise the publicly traded options at any time, but you may not sell the securities during a trading blackout period or at any time that you are aware of material nonpublic information.

24. *May I own shares of a mutual fund that invests in Alumis?*

A: Yes.

25. *Are mutual fund shares holding Alumis common stock subject to the trading blackout periods?*

A: No. You may trade in mutual funds holding Alumis common stock at any time.

26. *May I use a "routine trading program" or "10b5-1 plan"?*

A: Yes, subject to the requirements discussed in our insider trading policy and our 10b5-1 Trading Plan Guidelines. A routine trading program, also known as a 10b5-1 plan, allows you to set up a highly structured program with your stock broker where you specify ahead of time the date, price, and amount of securities to be traded. If you wish to create a 10b5-1 plan, please contact an attorney within our legal team .

27. *What happens if I violate our insider trading policy?*

A: Violating our policies may result in disciplinary action, which may include termination of your employment or other relationship with Alumis. In addition, you may be subject to criminal and civil sanctions.

28. *Who should I contact if I have questions about our insider trading policy or specific trades?*

A: You should contact an attorney within our legal department.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-280640) of Alumis Inc. of our report dated March 19, 2025 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 19, 2025

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS
ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Martin Babler, certify that:

1. I have reviewed this annual report on Form 10-K of Alumis Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements and other financial information included in this report, fairly present, in all material respects, the financial condition, results of operations, and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - c. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's Board of Directors:
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize, and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 19, 2025

/s/ Martin Babler

Name: Martin Babler

Title: Chief Executive Officer

(Principal Executive Officer)

**CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS
ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, John Schroer, certify that:

1. I have reviewed this annual report on Form 10-K of Alumis Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements and other financial information included in this report, fairly present, in all material respects, the financial condition, results of operations, and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - c. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's Board of Directors:
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize, and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 19, 2025

/s/ John Schroer

Name: John Schroer

Title: Chief Financial Officer

(Principal Financial and Accounting Officer)

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the “Exchange Act”) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Martin Babler, Chief Executive Officer of Alumis Inc. (the “Company”), hereby certifies that:

- (i) The Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2024, to which this Certification is attached as Exhibit 32.1 (the “Annual Report”), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
- (ii) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 19, 2025

By: /s/ Martin Babler

Name: Martin Babler

Title: Chief Executive Officer

(Principal Executive Officer)

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF
THE SARBANES-OXLEY ACT OF 2002**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the “Exchange Act”) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), John Schroer, Chief Financial Officer of Alumis Inc. (the “Company”), hereby certifies that:

- (i) The Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2024, to which this Certification is attached as Exhibit 32.2 (the “Annual Report”), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
- (ii) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 19, 2025

By: /s/ John Schroer

Name: John Schroer

Title: Chief Financial Officer

(Principal Financial and Accounting Officer)

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

ALUMIS, INC.

INCENTIVE COMPENSATION RECOUPMENT POLICY

1. INTRODUCTION

The Board of Directors (the “**Board**”) of Alumis, Inc., a Delaware corporation (the “**Company**”), has determined that it is in the best interests of the Company and its stockholders to adopt this Incentive Compensation Recoupment Policy (this “**Policy**”) providing for the Company’s recoupment of Recoverable Incentive Compensation that is received by Covered Officers of the Company under certain circumstances. Certain capitalized terms used in this Policy have the meanings given to such terms in Section 3 below.

This Policy is designed to comply with, and shall be interpreted to be consistent with, Section 10D of the Exchange Act, Rule 10D-1 promulgated thereunder (“**Rule 10D-1**”) and Nasdaq Listing Rule 5608 (the “**Listing Standards**”).

2. EFFECTIVE DATE

This Policy shall apply to all Incentive Compensation that is received by a Covered Officer on or after June 28, 2024 (the “**Effective Date**”). Incentive Compensation is deemed “**received**” in the Company’s fiscal period in which the Financial Reporting Measure specified in the Incentive Compensation award is attained, even if the payment or grant of such Incentive Compensation occurs after the end of that period.

3. DEFINITIONS

“**Accounting Restatement**” means an accounting restatement that the Company is required to prepare due to the material noncompliance of the Company with any financial reporting requirement under the securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements, or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period.

“**Accounting Restatement Date**” means the earlier to occur of (a) the date that the Board, a committee of the Board authorized to take such action, or the officer or officers of the Company authorized to take such action if Board action is not required, concludes, or reasonably should have concluded, that the Company is required to prepare an Accounting Restatement, or (b) the date that a court, regulator or other legally authorized body directs the Company to prepare an Accounting Restatement.

“**Administrator**” means the Compensation Committee or, in the absence of such committee, the Board.

“**Code**” means the U.S. Internal Revenue Code of 1986, as amended, and the regulations promulgated thereunder.

“**Compensation Committee**” means the Compensation Committee of the Board.

“**Covered Officer**” means each current and former Executive Officer.

“**Exchange**” means the Nasdaq Stock Market.

“**Exchange Act**” means the U.S. Securities Exchange Act of 1934, as amended.

“**Executive Officer**” means the Company’s president, principal financial officer, principal accounting officer (or if there is no such accounting officer, the controller), any vice-president of the Company in charge of a principal business unit, division, or function (such as sales, administration, or finance), any other officer who performs a policy-making function, or any other person who performs similar policy-making functions for the Company. Executive officers of the Company’s parent(s) or subsidiaries are deemed executive officers of the Company if they perform such policy-making functions for the Company. Policy-making function is not intended to include policy-making functions that are not significant. Identification of an executive officer for purposes of this Policy would include at a minimum executive officers identified pursuant to Item 401(b) of Regulation S-K promulgated under the Exchange Act.

“**Financial Reporting Measures**” means measures that are determined and presented in accordance with the accounting principles used in preparing the Company’s financial statements, and any measures derived wholly or in part from such measures, including Company stock price and total stockholder return (“**TSR**”). A measure need not be presented in the Company’s financial statements or included in a filing with the SEC in order to be a Financial Reporting Measure.

“**Incentive Compensation**” means any compensation that is granted, earned or vested based wholly or in part upon the attainment of a Financial Reporting Measure.

“**Lookback Period**” means the three completed fiscal years immediately preceding the Accounting Restatement Date, as well as any transition period (resulting from a change in the Company’s fiscal year) within or immediately following those three completed fiscal years (except that a transition period of at least nine months shall count as a completed fiscal year). Notwithstanding the foregoing, the Lookback Period shall not include fiscal years completed prior to the Effective Date.

“**Recoverable Incentive Compensation**” means Incentive Compensation received by a Covered Officer during the Lookback Period that exceeds the amount of Incentive Compensation that would have been received had such amount been determined based on the Accounting Restatement, computed without regard to any taxes paid (*i.e.*, on a gross basis without regard to tax withholdings and other deductions). For any compensation plans or programs that take into account Incentive Compensation, the amount of Recoverable Incentive Compensation for purposes of this Policy shall include, without limitation, the amount contributed to any notional account based on Recoverable Incentive Compensation and any earnings to date on that notional amount. For any Incentive Compensation that is based on stock price or TSR, where the Recoverable Incentive Compensation is not subject to mathematical recalculation directly from the information in an Accounting Restatement, the Administrator will determine the amount of Recoverable Incentive Compensation based on a reasonable estimate of the effect of the Accounting Restatement on the stock price or TSR upon which the Incentive Compensation was received. The Company shall maintain documentation of the determination of that reasonable estimate and provide such documentation to the Exchange in accordance with the Listing Standards.

“**SEC**” means the U.S. Securities and Exchange Commission.

4. RECOUPMENT

(a) **Applicability of Policy.** This Policy applies to Incentive Compensation received by a Covered Officer (i) after beginning services as an Executive Officer, (ii) who served as an Executive Officer at any time during the performance period for such Incentive Compensation, (iii) while the Company had a class of securities listed on a national securities exchange or a national securities association, and (iv) during the Lookback Period.

(b) **Recoupment Generally.** Pursuant to the provisions of this Policy, if there is an

Accounting Restatement, the Company must reasonably promptly recoup the full amount of the Recoverable Incentive Compensation, unless the conditions of one or more subsections of Section 4(c) of this Policy are met and the Compensation Committee, or, if such committee does not consist solely of independent directors, a majority of the independent directors serving on the Board, has made a determination that recoupment would be impracticable. Recoupment is required regardless of whether the Covered Officer engaged in any misconduct and regardless of fault, and the Company's obligation to recoup Recoverable Incentive Compensation is not dependent on whether or when any restated financial statements are filed.

(c) Impracticability of Recovery. Recoupment may be determined to be impracticable if, and only if:

(i) the direct expense paid to a third party to assist in enforcing this Policy would exceed the amount of the applicable Recoverable Incentive Compensation; provided that, before concluding that it would be impracticable to recover any amount of Recoverable Incentive Compensation based on expense of enforcement, the Company shall make a reasonable attempt to recover such Recoverable Incentive Compensation, document such reasonable attempt(s) to recover, and provide that documentation to the Exchange in accordance with the Listing Standards; or

(ii) recoupment of the applicable Recoverable Incentive Compensation would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the requirements of Code Section 401(a)(13) or Code Section 411(a) and regulations thereunder.

(d) Sources of Recoupment. To the extent permitted by applicable law, the Administrator shall, in its sole discretion, determine the timing and method for recouping Recoverable Incentive Compensation hereunder, provided that such recoupment is undertaken reasonably promptly. The Administrator may, in its discretion, seek recoupment from a Covered Officer from any of the following sources or a combination thereof, whether the applicable compensation was approved, awarded, granted, payable or paid to the Covered Officer prior to, on or after the Effective Date: (i) direct repayment of Recoverable Incentive Compensation previously paid to the Covered Officer; (ii) cancelling prior cash or equity-based awards (whether vested or unvested and whether paid or unpaid); (iii) cancelling or offsetting against any planned future cash or equity-based awards; (iv) forfeiture of deferred compensation, subject to compliance with Code Section 409A; and (v) any other method authorized by applicable law or contract. Subject to compliance with any applicable law, the Administrator may effectuate recoupment under this Policy from any amount otherwise payable to the Covered Officer, including amounts payable to such individual under any otherwise applicable Company plan or program, *e.g.*, base salary, bonuses or commissions and compensation previously deferred by the Covered Officer. The Administrator need not utilize the same method of recovery for all Covered Officers or with respect to all types of Recoverable Incentive Compensation.

(e) No Indemnification of Covered Officers. Notwithstanding any indemnification agreement, applicable insurance policy or any other agreement or provision of the Company's certificate of incorporation or bylaws to the contrary, no Covered Officer shall be entitled to indemnification or advancement of expenses in connection with any enforcement of this Policy by the Company, including paying or reimbursing such Covered Officer for insurance premiums to cover potential obligations to the Company under this Policy.

(f) Indemnification of Administrator. Any members of the Administrator, and any other members of the Board who assist in the administration of this Policy, shall not be personally liable for any action, determination or interpretation made with respect to this Policy and shall be indemnified by the

Company to the fullest extent under applicable law and Company policy with respect to any such action, determination or interpretation. The foregoing sentence shall not limit any other rights to indemnification of the members of the Board under applicable law or Company policy.

(g) **No “Good Reason” for Covered Officers.** Any action by the Company to recoup or any recoupment of Recoverable Incentive Compensation under this Policy from a Covered Officer shall not be deemed (i) “good reason” for resignation or to serve as a basis for a claim of constructive termination under any benefits or compensation arrangement applicable to such Covered Officer, or (ii) to constitute a breach of a contract or other arrangement to which such Covered Officer is party.

5. ADMINISTRATION

Except as specifically set forth herein, this Policy shall be administered by the Administrator. The Administrator shall have full and final authority to make any and all determinations required under this Policy. Any determination by the Administrator with respect to this Policy shall be final, conclusive and binding on all interested parties and need not be uniform with respect to each individual covered by this Policy. In carrying out the administration of this Policy, the Administrator is authorized and directed to consult with the full Board or such other committees of the Board as may be necessary or appropriate as to matters within the scope of such other committee’s responsibility and authority. Subject to applicable law, the Administrator may authorize and empower any officer or employee of the Company to take any and all actions that the Administrator, in its sole discretion, deems necessary or appropriate to carry out the purpose and intent of this Policy (other than with respect to any recovery under this Policy involving such officer or employee).

6. SEVERABILITY

If any provision of this Policy or the application of any such provision to a Covered Officer shall be adjudicated to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other provisions of this Policy, and the invalid, illegal or unenforceable provisions shall be deemed amended to the minimum extent necessary to render any such provision or application enforceable.

7. NO IMPAIRMENT OF OTHER REMEDIES

Nothing contained in this Policy, and no recoupment or recovery as contemplated herein, shall limit any claims, damages or other legal remedies the Company or any of its affiliates may have against a Covered Officer arising out of or resulting from any actions or omissions by the Covered Officer. This Policy does not preclude the Company from taking any other action to enforce a Covered Officer’s obligations to the Company, including, without limitation, termination of employment and/or institution of civil proceedings. This Policy is in addition to the requirements of Section 304 of the Sarbanes-Oxley Act of 2002 (“**SOX 304**”) that are applicable to the Company’s Chief Executive Officer and Chief Financial Officer and to any other compensation recoupment policy and/or similar provisions in any employment, equity plan, equity award, or other individual agreement, to which the Company is a party or which the Company has adopted or may adopt and maintain from time to time; provided, however, that compensation recouped pursuant to this Policy shall not be duplicative of compensation recouped pursuant to SOX 304 or any such compensation recoupment policy and/or similar provisions in any such employment, equity plan, equity award, or other individual agreement except as may be required by law.

8. AMENDMENT; TERMINATION

The Administrator may amend, terminate or replace this Policy or any portion of this Policy at any time and from time to time in its sole discretion. The Administrator shall amend this Policy as it deems necessary to comply with applicable law or any Listing Standard.

9. SUCCESSORS

This Policy shall be binding and enforceable against all Covered Officers and, to the extent required by Rule 10D-1 and/or the applicable Listing Standards, their beneficiaries, heirs, executors, administrators or other legal representatives.

10. REQUIRED FILINGS

The Company shall make any disclosures and filings with respect to this Policy that are required by law, including as required by the SEC.

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ALUMIS, INC.

INCENTIVE COMPENSATION RECOUPMENT POLICY

FORM OF EXECUTIVE ACKNOWLEDGMENT

I, the undersigned, agree and acknowledge that I am bound by, and subject to, the Alumis, Inc. Incentive Compensation Recoupment Policy, as may be amended, restated, supplemented or otherwise modified from time to time (the "**Policy**"). In the event of any inconsistency between the Policy and the terms of any employment agreement, offer letter or other individual agreement with Alumis, Inc. (the "**Company**") to which I am a party, or the terms of any compensation plan, program or agreement, whether or not written, under which any compensation has been granted, awarded, earned or paid to me, the terms of the Policy shall govern.

In the event that the Administrator (as defined in the Policy) determines that any compensation granted, awarded, earned or paid to me must be forfeited or reimbursed to the Company pursuant to the Policy, I will promptly take any action necessary to effectuate such forfeiture and/or reimbursement. I further agree and acknowledge that I am not entitled to indemnification, and hereby waive any right to advancement of expenses, in connection with any enforcement of the Policy by the Company.

Agreed and Acknowledged:

Name: _____

Title: _____

Date: _____
