ALTO NEUROSCIENCE

# 2024 Annual Report

The future of psychiatry is precision



**Alto Neuroscience**
650 Castro Street, Suite 450
Mountain View, CA 94041

Dear Stockholders,

This past year has been transformational for Alto, marked by our initial public offering and the completion of several crucial milestones across our pipeline. We continued to deepen our understanding of neurobiological processes in defined patient subtypes, incorporated key learnings across our ongoing clinical trials to improve the probability of success, and advanced tools that we believe underscore the promise of precision psychiatry. As a scientific founder with a sincere passion to move the field forward, I am proud of all we have accomplished in our efforts to transform groundbreaking science into potentially meaningful solutions for patients.

Alto was founded in 2019 to help patients with neuropsychiatric conditions achieve better outcomes by developing personalized and more effective treatment options. The current trial-and-error approach, where treatments are given without considering the heterogeneity and biological differences among patients, underscores the pressing need for innovation in psychiatry. Our work today builds on 15 years of foundational research, focused on identifying key brain biomarkers and developing analytical methods to derive the underlying biology of psychiatric conditions. Leveraging these deep insights, and with an unwavering commitment to improving clinical impact, we have set out to reimagine how psychiatric treatments are both developed and deployed. Using our proprietary platform, we have collected brain-based biomarkers in over 2,000 participants and have now completed six clinical studies across our pipeline programs.

To strengthen our foundation, we have carefully curated a group of dedicated, mission-driven leaders who are not only experts in their fields but also deeply aligned with our vision. In parallel, Alto remains steadfast in pursuing opportunities for growth to maximize the therapeutic impact of our platform and address the high unmet needs of patients. This includes ongoing partnership discussions and novel testing methods that we believe will continue to redefine how psychiatric conditions are understood, diagnosed, and treated.

We believe the coming years hold tremendous promise and with a strong balance sheet to support several key clinical milestones, we are well positioned to achieve our ambitious objectives. Our unwavering focus remains on delivering value—for our stockholders and for the patients who inspire our work every day. On behalf of the entire team, thank you for your partnership and support. We look forward to continuing this journey and are highly motivated to deliver on the promise of precision medicine in psychiatry.

Warm Regards,



Amit Etkin, MD, PhD
Founder, President, and Chief Executive Officer

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

# FORM 10-K

**(Mark One)**

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

**For the fiscal year ended December 31, 2024**

**OR**

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

**Commission file number 001-41944**

# Alto Neuroscience, Inc.

(Exact Name of Registrant as Specified in Its Charter)

| **Delaware** | **83-4210124** |
|---|---|
| (State or Other Jurisdiction of Incorporation or Organization) | (I.R.S. Employer Identification No.) |
| **650 Castro Street, Suite 450 Mountain View, CA** | **94041** |
| (Address of Principal Executive Offices) | (Zip Code) |

**(650) 200-0412**
Registrant's telephone number, including area code

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

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, $0.0001 par value per share | ANRO | New York Stock Exchange |

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

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

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

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

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

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

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☐ |
| Non-accelerated filer | ☒ | Smaller reporting company | ☒ |
| | | Emerging growth company | ☒ |

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

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

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

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

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

As of June 30, 2024, the aggregate market value of the registrant's Common Stock held by non-affiliates was $266.5 million.

The number of shares of registrant's Common Stock outstanding as of March 17, 2025 was 27,072,129.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to the 2025 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K. The Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the year ended December 31, 2024.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this Annual Report, including statements regarding our plans, objectives, goals, strategies, future events, future revenues or performance, financing needs, plans, or intentions relating to product candidates and markets and business trends are forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "can," "contemplate," "continue," "could," "design," "estimate," "expect," "intend," "may," "might," "objective," "plan," "potential," "predict," "project," "shall," "should," "target," "will," or "would," or the negative of these words or other similar terms or expressions.

These statements involve known and unknown risks, uncertainties, and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress, and results of our research and development programs, preclinical studies, any clinical trials, and IND and other regulatory submissions;
- the ability of our approach to reproducibly predict treatment outcomes for product candidates amongst identified patient populations and achieve clinical success;
- our ability to continue to identify appropriate biomarkers for use in further clinical development;
- the timing of and costs involved in obtaining and maintaining regulatory approval of our current product candidates and any future product candidates that we may identify or develop;
- the beneficial characteristics, including potential safety, efficacy, and therapeutic effects, of our product candidates;
- our ability to efficiently and cost-effectively conduct our current and future clinical trials;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates, if approved;
- our ability to maintain existing, and establish new, strategic collaborations, licensing, or other arrangements, including our ability to comply with our financial obligations pursuant to the terms of such agreements;
- the timing and likelihood of the achievement of milestones pursuant to our existing collaboration and licensing agreements;
- our ability to identify and develop product candidates for treatment of additional indications;
- the performance of our third-party service providers, including our suppliers and manufacturers;
- the rate and degree of market acceptance and clinical utility for our current product candidates and any other product candidates we may develop;
- the effects of competition with respect to our current product candidates or any of our future product candidates, as well as innovations by current and future competitors in our industry;
- our estimates regarding the potential market opportunities and the number of patients for our product candidates and any future product candidates, if approved for commercial use;
- the implementation of our strategic plans for our business, any product candidates we may develop;
- our intellectual property position, including the scope of protection we are able to establish, maintain, defend and enforce for intellectual property rights covering our product candidates and our Precision Psychiatry Platform;
- our ability to attract and retain key scientific or management personnel;

- regulatory and legal developments in the United States and foreign countries;
- our ability to attract and retain employees and collaborators with development, regulatory, and commercialization expertise;
- our ability to comply with the terms of our loan agreements and our expectations regarding our ability to access additional tranches thereunder;
- the accuracy of our estimates regarding future expenses, future revenue, capital requirements, and need for additional financing;
- the anticipated impact of global economic uncertainty, financial market conditions and geopolitical events, including the conflict between Ukraine and Russia, the regional conflict in the Middle East, geopolitical tensions in China, high levels of inflation, fluctuating interest rates, and proposed tariffs on our business, results of operations, and financial condition;
- the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements; and
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

These forward-looking statements reflect our management's beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this Annual Report and are subject to risks and uncertainties. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while 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 an exhaustive 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.

You are urged to carefully review the disclosures we make concerning risks and other factors that may affect our business and operating results under "Item 1A. Risk Factors" in this Annual Report, as well as our other reports filed with the Securities and Exchange Commission, or SEC. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in such statements. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

Any public statements or disclosures by us following this Annual Report that modify or impact any of the forward-looking statements contained in this Annual Report will be deemed to modify or supersede such statements in this Annual Report. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events, or otherwise.

We routinely use our investor relations website to post presentations to investors and other important information, including information that may be material. Accordingly, we encourage investors and others interested in Alto to review the information it makes public on its investor relations website.

## Part I

### Item 1. Business.

#### Overview

We are a clinical-stage biopharmaceutical company with a mission to redefine psychiatry by leveraging neurobiology to develop personalized and highly effective treatment options. Through insights derived from our scalable and proprietary Precision Psychiatry Platform, or our Platform, we aim to discover brain-based biomarkers to better identify which patients are more likely to respond to our novel product candidates. Our current pipeline consists of five clinical-stage assets addressing high-need therapeutic areas, including major depressive disorder, or MDD, bipolar depression, or BPD, and schizophrenia. Our most advanced programs are supported by prospectively replicated evidence of clinical activity in biomarker-characterized populations.

Mental health conditions are a leading cause of disability globally. In the United States, current estimates suggest that 13% of adults take antidepressants and over 50% of the population will be diagnosed with a psychiatric disorder during their lifetime, with an estimated $280 billion spent on mental health services in 2020. We believe limitations of currently available treatments, which are often ineffective in a large portion of patients, are a key driver of these rising costs. We believe better outcomes can be achieved through precision medications tailored specifically to address heterogenous alterations in brain functioning seen across individual patients within any psychiatric diagnosis.

While personalized medicine has made significant advances in other areas, most notably in oncology, neuropsychiatry drug development and patient treatment remain largely untargeted. Alto was founded in 2019 to drive innovation in psychiatry and disrupt the traditional, all-comer approach to central nervous system, or CNS, drug development and clinical care. Our precision approach harnesses deep neurobiological insights to identify and develop personalized, highly effective and clinically differentiated treatment options in stratified populations to improve patient outcomes. We believe the opportunity across our portfolio represents a potential to impact over 25 million patients in the United States alone.

#### Our Platform

Our Platform employs modern tools for measuring human neurobiology and rigorous data science analytics. By combining inputs and expertise across multiple domains, we designed a platform that enables the integration and in-depth analysis of disparate data sets from a variety of sources. The initial development and refinement process involved specialists in data science, software engineering, neuroscience, and psychiatry; and we continue to expand and improve our Platform as we collect additional data across our clinical-stage programs. We believe the neuropsychiatry domain expertise leveraged to develop our Platform provides a distinct advantage in our ability to discover and develop biomarkers that are highly relevant to underlying brain circuit function.

Using our Platform, we collect and analyze data from neurocognitive assessments, electroencephalography, or EEG, and wearable devices. We also collect data from genetic and genomic samples. With our Platform, we employ quantitative analytics, including machine learning, to discover and evaluate unique biomarkers. Our approach aims to avoid the need for interpretation of biomarker data by a clinician, thereby enabling seamless integration into current clinical practice. The Platform is designed for commercial scalability, emphasizing the use of reliable and reproducible biomarkers that can be easily collected in any patient care setting without significant logistical or financial burden. The potential scalability of our Platform has been demonstrated through biomarker collection across more than 70 unique clinical sites and from over 2,000 participants.

#### Our Strategy

We are building a leading precision psychiatry company with a mission to redefine neuropsychiatric care with personalized and highly effective treatment options. We intend to accomplish our mission by implementing the following key strategies.

*Leverage our Platform to advance the first biomarker-driven pipeline for neuropsychiatric indications*

- Our Platform generates biological and clinical insights that are rarely, if ever, gained through traditional CNS drug development approaches, which directly guide each phase of the drug development process.
- We aim to use these unique insights to advance our current pipeline products and increase the probability of success for our portfolio of differentiated drug candidates designed to target independent, biomarker-defined patient populations with high unmet needs.

*Discover and prospectively replicate objective biomarkers for patient selection*

- Our proprietary approach relies on rigorous analytics using patient-derived data to discover, and prospectively replicate, biomarker signatures for likely drug responders. In addition to identifying likely drug responders, we deploy our Platform in early-stage clinical development to characterize drug effects on the brain.

*Leverage our internal clinical operations and software development expertise*

- We believe our in-house model creates synergies between trials, and enables us to conduct multiple studies simultaneously, reduce cost, and apply learnings across programs to enhance execution.
- Our approach to data oversight enables us to design software tools, such as Spectra, TechCheck, and Altoscope, which are tailored to the requirements of our biomarker data collection with an understanding of how these data will ultimately be gathered in clinical practice.

*Expand our pipeline by strategically evaluating in-licensing and acquisition opportunities.*

- We plan to seek opportunities to in-license, acquire, or partner on new product candidates in clinical indications where we are able to offer unique expertise to potentially enhance the product candidate's value and potentially streamline development through targeted patient selection.

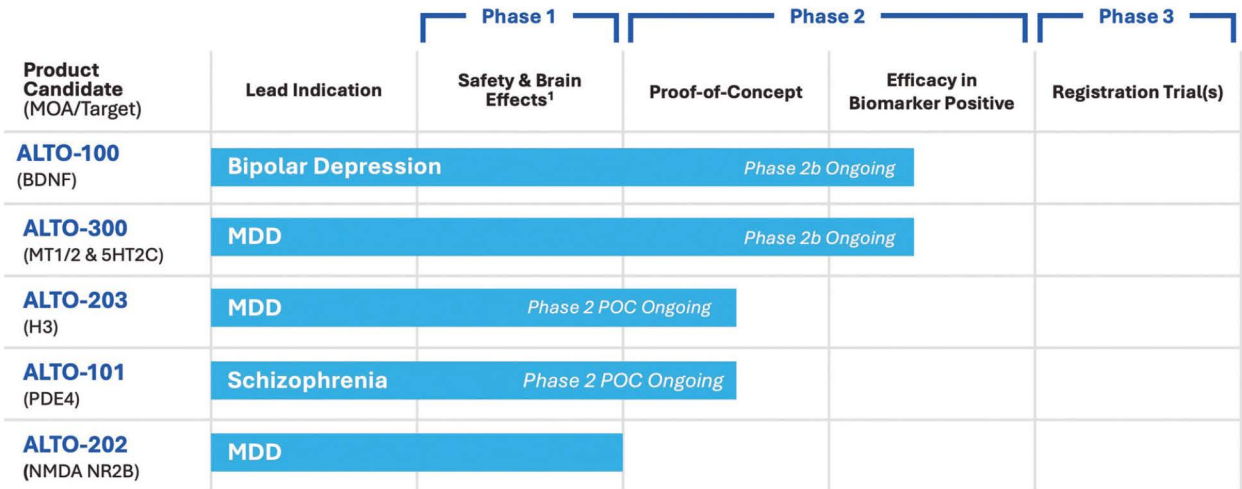
*Selectively partner our product candidates to maximize their value to patients and our stockholders.*

- As we advance the development of our product candidates, in addition to internal commercial capabilities that we may establish, we may also selectively partner with global pharmaceutical companies to maximize the value of our targeted product candidates and robust intellectual property portfolio.
- We may seek partnerships where the efficiency of development and/or the commercial infrastructure required is best achieved through external capabilities.

## Our Product Candidates

Our clinical-stage product candidates are being advanced based on extensive preclinical and clinical data that suggest the potential to bring significant improvements to patient populations not adequately treated with current standard-of-care medications.

Our pipeline of clinical-stage product candidates is depicted below:




**BDNF: Brain Derived Neurotrophic Factor; MDD: Major Depressive Disorder; MT1/2: Melatonin Receptor 1 and 2; 5-HT2C: 5-Hydroxytriptamine Receptor 2C; H3: Histamine H3 Receptor; PDE4: Phosphodiesterase-4; NMDA NR2B: N-methyl-D-aspartate Receptor Subtype 2B**

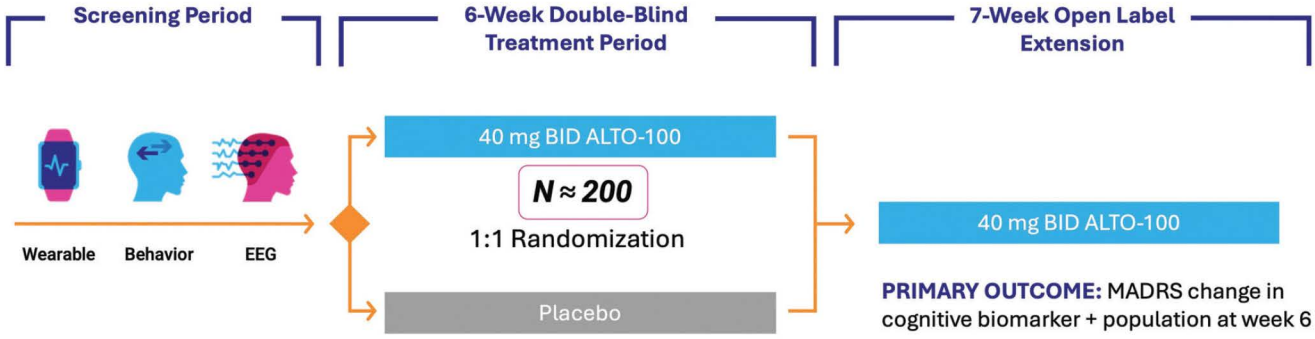
[1]We have active investigational new drug applications, or INDs, for each of ALTO-100, ALTO-300, ALTO-203, ALTO-101, and ALTO-202 in the indications listed. ALTO-100, ALTO-203, ALTO-101, and ALTO-202 were evaluated in Phase 1 safety trials by their respective originators prior to our acquisition or licensing of the product candidate.

***ALTO-100***

*Overview*

ALTO-100 is a novel small molecule that has shown evidence of a pro-neurogenesis/neuroplasticity mechanism of action, and we believe binds a receptor not targeted by other CNS therapeutics, which would make it first-in-class if approved.

We are currently evaluating ALTO-100 in a Phase 2b trial in patients with BPD, in which patients are assigned to take ALTO-100 as adjunctive treatment to a stable dose of a background mood stabilizing treatment over a 6-week treatment period. BPD is associated with memory, cognitive, and neuroplasticity abnormalities at similar or greater rates than seen in MDD. Much like MDD, poor memory and cognition patients typically experience greater treatment resistance and disability, with overall worse outcomes. Moreover the only currently approved therapies are antipsychotics. We believe the pro-neuroplasticity mechanism of ALTO-100 has the potential to address the high unmet need in this important patient population. The design of the trial is depicted below.




Enrollment in this trial is ongoing, with a target of approximately 200 patients, and we expect to report topline data from the study in the second half of 2026.

In July 2024 we reported that this Phase 2b study is supported in part by a funding award from The Wellcome Trust Limited, or Wellcome. See "—License and Other Agreements—The Wellcome Trust Limited Convertible Grant Agreement" for additional information.

We have granted patents and pending patent applications that we believe provide protection of ALTO-100 to at least 2043. In particular, our development of ALTO-100 in the United States is protected by granted patents covering methods of treating BPD and MDD in patients having objectively determined impaired learning and/or memory with 40-240 mg of ALTO-100. As granted, not accounting for any potential patent term extensions, the patents are expected to cover the use of ALTO-100 in the specified patient population until 2043.

*Background on ALTO-100*

Deficits in neuroplasticity lead to reductions in an individual's ability to effectively adapt to their environment, which in patients with depression reinforces negative thought and behavioral patterns. Reductions in plasticity-promoting signaling molecules, such as brain derived neurotrophic factor, or BDNF, are also seen in the hippocampus of patients with depression, giving rise to a "neurotrophin hypothesis of depression" in which a central component is the resulting hippocampal neuroplasticity impairment. BDNF plays key roles in neuroplasticity at the synaptic and cellular levels, as well at the level of hippocampal neurogenesis, or the process of forming new neurons in the adult brain. ALTO-100 has demonstrated enhanced hippocampal neuroplasticity at the synaptic and cellular levels, along with neurogenesis, which we believe suggests the potential to ameliorate depression symptoms in patients with this disruption, identified clinically as deficits in hippocampus-dependent verbal memory.

*Our Completed ALTO-100 Phase 2b Trial in MDD*

In October 2024, we announced that our Phase 2b study of ALTO-100 in patients with MDD did not meet its primary endpoint, assessed by a change from baseline in Montgomery-Åsberg Depression Rating Scale, or MADRS, compared to placebo. The topline results included the primary and key secondary analyses in the biomarker positive modified-intent-to-treat, or mITT, population which included monotherapy and adjunctive treatment populations combined (n=196) and the

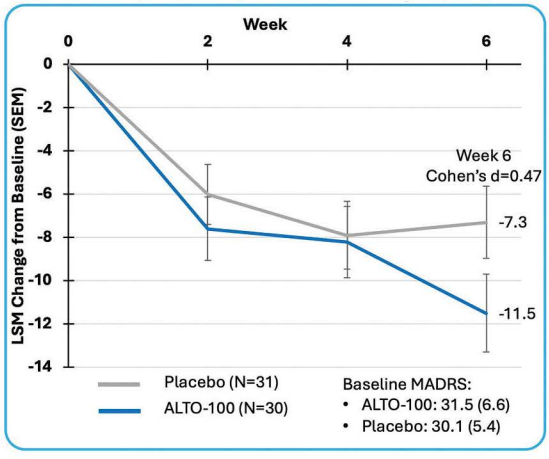
monotherapy population alone (n=135) respectively. We further reported that the favorable safety and tolerability profile of ALTO-100 was consistent with previously reported studies. Overall, placebo response was well-managed, and the biomarker did not enrich for a larger placebo response in the study. The primary and pre-specified key secondary analyses are depicted in the table below.

| ALL ANALYSIS POPULATION | SAMPLE SIZE (N) | | MEAN BASELINE MADRS (SD) | | WEEK 6 LSM MADRS CHANGE (SE) | | COHEN'S D | P |
|---|---|---|---|---|---|---|---|---|
| | ALTO-100 | Placebo | ALTO-100 | Placebo | ALTO-100 | Placebo | | |
| **ALL BIO + MITT** *(PRIMARY)* | 97 | 99 | 31.2(5.4) | 31.5(5.4) | -10.3(1.0) | -9.8(1.0) | 0.05 | >0.1 |
| **MONOTHERAPY BIO + MITT** *(KEY SECONDARY)* | 67 | 68 | 31.0(4.8) | 32.2(5.3) | -9.9(1.2) | -11.1(1.1) | -0.13 | >0.1 |
| **ADJUNCTIVE BIO + MITT** *(PRE-SPECIFIED SECONDARY, NOT POWERED)* | 30 | 31 | 31.5(6.6) | 30.1(5.4) | -11.5(1.8) | -7.3(1.7) | 0.47 | 0.09 |

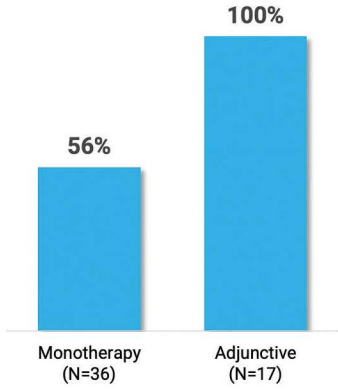
LSM: Least Squares Mean; SD: Standard Deviation; SE: Standard Error; BIO+: Biomarker Positive; MITT: Modified Intention to treat

In a pre-specified analysis of biomarker positive patients taking ALTO-100 or placebo adjunctively to a stable background antidepressant (n=61), ALTO-100 demonstrated a clinically meaningful effect compared to placebo at week 6 (Cohen's d=0.47, p=0.09). The pre-specified analysis of this population was not powered to achieve statistical significance.

**Clear drug effect in prespecified adjunctive population**




**Compliance rate among monotherapy and adjunctive patients in PK sample***

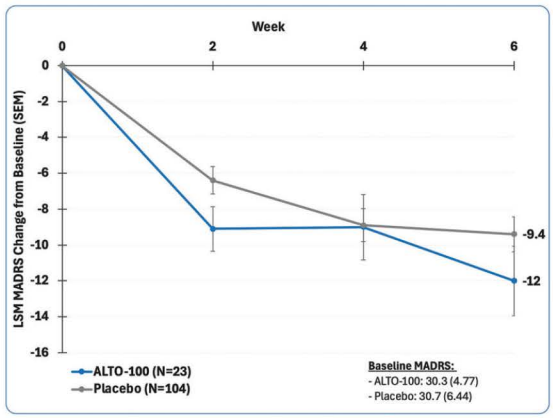



**Only a subset of sites within the study were setup to evaluate PK levels*

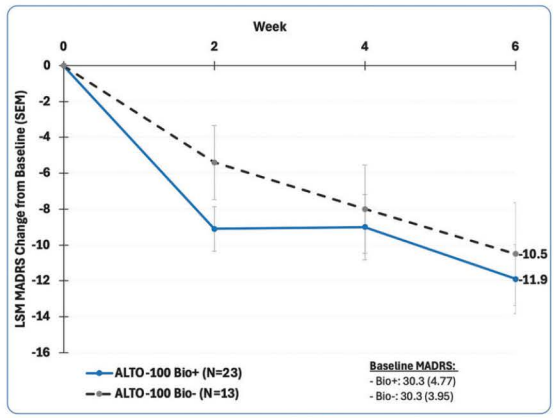
We believe the inconsistency of the ALTO-100 effect between the monotherapy population and the adjunctive population was due to a higher than anticipated level of non-compliance with study medication in the monotherapy group, while the adjunctive group demonstrated a high level of compliance (56% in monotherapy vs. 100% in adjunctive). The graph above (right panel) demonstrates the difference in compliance (as measured by detectable levels of ALTO-100 in blood samples) between the monotherapy and adjunctive populations.

In the subset of patients that had evidence of taking ALTO-100 through blood sample analysis, a greater improvement was observed with ALTO-100 compared to placebo in the patients with the cognitive biomarker (shown below on left), and the patients with the cognitive biomarker demonstrated a greater improvement than those without the biomarker (right). The analyses in the pharmacokinetic, or PK, positive sample are supportive of the overall potential efficacy of ALTO-100 in patients with the cognitive biomarker.

**Bio + confirmed compliant patients vs. all placebo**




**Bio + vs. bio – in confirmed compliant patients**




We believe the clinically meaningful signal in the adjunctive subgroup, combined with the evidence of biomarker enrichment in the compliant subset of patients, supports continuing the Phase 2b trial of ALTO-100 as an adjunctive treatment in BPD. Further, we believe the evidence across analyses of the ALTO-100 Phase 2b MDD trial broadly supports our enrichment approach as having the potential to identify patients that could demonstrate a better response to treatment.

### *ALTO-300*

*Overview*

ALTO-300 is an investigational oral, small molecule melatonergic (MT1 and MT2) agonist and serotonergic (5-HT2C) antagonist with antidepressant properties. We are developing ALTO-300 as an adjunctive treatment in the United States for patients with MDD, characterized by an EEG biomarker. The compound has been approved as an antidepressant in Europe and Australia with the International Nonproprietary Name, agomelatine.

In June 2023, we initiated a six-week, double-blind, placebo-controlled, randomized Phase 2b clinical trial in patients with MDD characterized by an EEG biomarker signature. We expect to enroll approximately 200 biomarker positive patients in the final analysis sample, which is therefore expected to result in approximately 320 patients enrolled in the study in total (inclusive of biomarker negative patients and patients not included in the final analysis sample as a result of the completed blinded site and patient case review). Patients are randomized to receive either 25mg of ALTO-300 once daily before bedtime, or QHS, or placebo in addition to a background antidepressant, to which they have had inadequate response, over a six-week treatment period. Patients are then enrolled into an eight-week open-label extension in which they receive 25mg QHS of ALTO-300. The primary endpoint in the trial is the change in MADRS score from baseline to week six in the EEG biomarker positive group. We expect to report topline data from this trial in mid-2026.

The ALTO-300 biomarker—a measure of reduced neural signaling stability—has been replicated and reverse translated to animals to elucidate a mechanistic link. In the preclinical model, administration of a 5-HT2C agonist led to a dose-related increase in EEG irregularity using the same measure as the human biomarker. Building on these results, we have now demonstrated the successful standardization of EEG enrichment marker acquisition through a platform that facilitates the identification of patients potentially most likely to respond to ALTO-300. Given the prevalence of patients with the biomarker profile observed in our clinical trials to date, we estimate approximately 50% of patients with MDD, to be eligible candidates for potential treatment with ALTO-300 if approved.

We have a granted patent and pending patent applications that we believe provide protection of ALTO-300 to at least 2044. In particular, our development of ALTO-300 in the United States is protected by a granted patent covering the use of ALTO-300 as an adjunctive therapy and patient selection using our EEG biomarker. As granted, not accounting for any potential patent term extensions, the patent is expected to cover the use of ALTO-300 in the EEG-defined patient population until 2044.

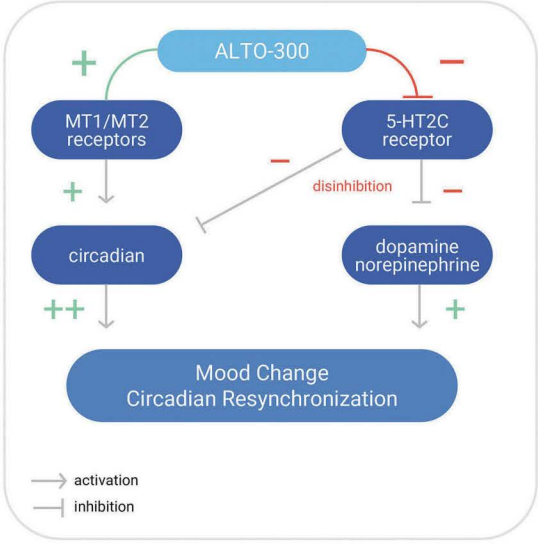
*MDD Background*

MDD is a psychiatric disorder characterized by key symptoms such as low mood, anhedonia, poor concentration and decision-making, and changes in sleep and appetite. It is one of the most common and debilitating medical disorders and, according to the World Health Organization, is a leading cause of disability worldwide. According to the National Institute of Mental Health, an estimated 8.3% of adults in the United States experienced one major depressive episode in 2021.

Given the extensive utilization of antipsychotic medications in depression, which are typically poorly tolerated, and the favorable tolerability profile of agomelatine, we believe the opportunity for a treatment with a novel mechanism in an adjunctive treatment population could provide a substantial benefit to patients and providers.

*Background on ALTO-300 (Agomelatine) and History of Clinical Development*

ALTO-300 is a product candidate known as agomelatine, initially developed by Servier. Agomelatine is a melatonergic (MT1 and MT2) agonist and serotonergic (5-HT2C) antagonist that is approved and commercially available in Europe (for the treatment of major depressive episodes in adults) and Australia (for the treatment of major depression in adults including prevention of relapse). As illustrated in the figure below, its MT1/2 agonism is thought to elevate mood through effects on circadian rhythms, while its 5-HT2C antagonism is thought to elevate mood by disinhibiting dopamine and norepinephrine release, particularly in the frontal cortex. This unique pattern of pharmacological activity is thought to contribute to agomelatine's favorable tolerability data, characterized by a low reported incidence of canonical antidepressant side effects such as gastrointestinal intolerability, anxiety, sleep disturbance, and sexual dysfunction. Compared to other adjunctive treatments, agomelatine has demonstrated similar all-comer efficacy and favorable tolerability, with no difference in dropout due to adverse events, unlike many antipsychotics. Further, agomelatine has been shown to better treat anhedonia symptoms as compared to selective serotonin reuptake inhibitors, or SSRIs, or serotonin-norepinephrine reuptake inhibitors, or SNRIs, in third-party clinical trials.




Agomelatine has been studied in thousands of patients globally, including a Phase 3 clinical development program for MDD in the United States by Novartis. In these studies, the observed antidepressant effects of 25mg and 50mg agomelatine were approximately similar. However, higher rates of reversible liver enzyme elevation have been observed in the 50mg relative to the 25mg dose, both in Servier's studies and in clinical practice. We are developing only 25mg agomelatine as ALTO-300.

*Interim Analysis Outcome from Ongoing Phase 2b Trial in MDD*

In February 2025, we announced a favorable outcome from the planned interim analysis for the Phase 2b trial of ALTO-300 as an adjunctive treatment for patients with MDD. The interim analysis resulted in a recommendation to continue the study with a total targeted biomarker positive population of approximately 200 patients in the final analysis sample. The original target sample was 150 biomarker positive patients. We believe increasing the biomarker positive sample improves the overall probability of success of this trial.

Prior to the interim analysis, a blinded committee conducted an in-depth site and patient eligibility review that resulted in the prospective exclusion of sites and patients from the analysis population. Following the eligibility review, the biomarker positive population in the interim analysis consisted of 87 patients.

*Our Completed ALTO-300 Phase 2a Trial in MDD*

We completed an exploratory Phase 2a clinical trial of ALTO-300 as an adjunctive treatment in patients with MDD who experienced inadequate response to an antidepressant. The eight-week clinical trial was conducted across more than 20 sites in the United States and enrolled 239 patients with MDD between the ages of 18-74 years old to evaluate potential predictive biomarkers as well as the efficacy and safety of ALTO-300. Patients remained on a background antidepressant and were administered 25mg of ALTO-300 once daily before bedtime. A total of 110 of these patients underwent EEG recordings, of which 105 met pre-specified eligibility requirements to be included in the EEG analyses. The primary analysis was change in depressive symptoms as measured by MADRS at week four.

The Phase 2a trial identified a reproducible, readily scalable, and easily administered machine learning-derived EEG biomarker, which was further validated through prospective replication. Significantly more biomarker-characterized patients (n=55) than patients without the biomarker (n=50) achieved clinical response (defined as ≥50% reduction in depression symptoms) at week four (47% vs. 28%), week six (58% vs. 34%), and week eight (62% vs. 48%) of treatment. Overall, we observed a robust clinical response in biomarker positive patients. Further, the predictive biomarker is specific to patients receiving ALTO-300, as it is not predictive of response in patients taking either placebo or standard-of-care SSRI/SNRIs based on data from separate studies in which EEG measurements allowed Alto to differentiate between patients with or without this EEG biomarker.

ALTO-300 was well tolerated in the Phase 2a trial among 239 patients, with no treatment-related serious adverse events reported. Importantly, we did not observe any incidents of liver function test, or LFT, elevations across aspartate transaminase or alanine transaminase greater than three times the upper limit of normal.

***ALTO-203***

*Overview*

ALTO-203 is an investigational, novel, oral small molecule histamine H3 receptor inverse agonist. We are currently advancing ALTO-203 for the treatment of patients with MDD associated with increased levels of anhedonia.

We are currently running a Phase 2 proof-of-concept, or POC, trial which consists of two sequential double-blind, placebo-controlled treatment periods with two dose levels of ALTO-203 as a monotherapy. In the first period, patients receive a single-dose of ALTO-203 or placebo, and the outcome measure is designed to evaluate pharmacodynamic effects. An acute change in positive emotion will be assessed by the alertness and mood components of the Bond-Lader Visual Analog Scale (BL-VAS), an established scale of subjective emotion also used in a prior Phase 1 trial of ALTO-203. In the second period, patients receive ALTO-203 or placebo once daily over a 28-day treatment period to evaluate the clinical activity and safety of ALTO-203. The study is powered based on the outcomes being evaluated in the first period. The clinical outcomes, e.g., MADRS, are not powered to detect statistical significance. We have completed enrollment with 69 patients in the study and expect to report topline data in the second quarter of 2025.

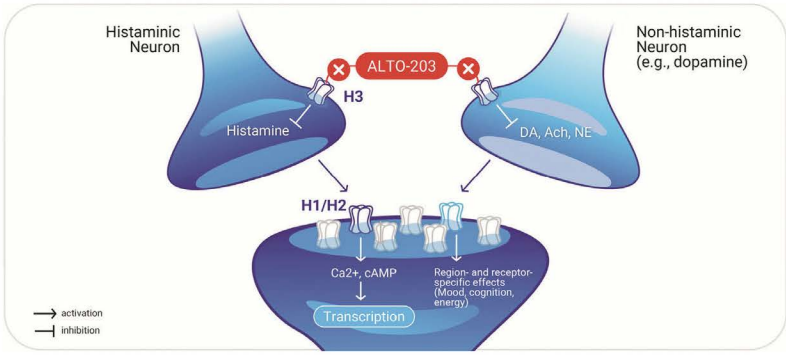
Our development of ALTO-203 is protected by a robust intellectual property estate, including granted patents and pending patent applications. We believe our patent applications for ALTO-203 will provide protection to at least 2044.

*MDD with Anhedonia Background*

Symptoms of reduced experience of pleasure or motivation to engage in rewarding activities, termed anhedonia, are a common component of many neuropsychiatric disorders. In MDD, anhedonia is associated with poorer treatment response, as well as greater chronicity and disability. Neurobiological studies have suggested that reductions in dopamine release and/or dopaminergic signaling in the reward system, inclusive of the nucleus accumbens, may contribute to anhedonia. As such, a drug that enhances nucleus accumbens dopamine release may prove to be a particularly fruitful approach to treating anhedonia, as well as related depressive symptoms. Moreover, an increase in reward system dopamine may have beneficial effects on elements of cognition in these patients, essentially by increasing motivational processes. Anhedonia is a common symptom, reported in more than 75% of people with depression.

*Background on ALTO-203*

The histamine H3 receptor, unlike other histamine receptors, is located predominantly in the brain and acts as a master regulator, inhibiting the release of a number of other major neurotransmitters including histamine, dopamine, acetylcholine, and norepinephrine. By inhibiting the "brake" driven through tonic activity the H3 receptor, levels of these neurotransmitters are thought to increase. Use of an H3 inverse agonist may therefore be important given its potential to block both histamine-induced and basal levels of receptor activity. The figure below illustrates the potential mechanism of action of ALTO-203.




Despite these theoretical effects of blocking H3 receptors, as well as the action of many H3 inverse agonists on cortical dopamine release, prior data on several H3 inverse agonists have failed to demonstrate any effects on dopamine release in the nucleus accumbens. This lack of an effect on dopamine is particularly notable for the only approved H3 inverse agonist, pitolisant, which is indicated for the treatment of excessive daytime sleepiness in narcolepsy. In a preclinical study conducted by ALTO-203's originator, ALTO-203 demonstrated an elevation of dopamine in the nucleus accumbens, a region of the brain thought to be particularly implicated for reward and motivation. We believe this activity in the nucleus accumbens differentiates ALTO-203 from other H3 inverse agonists given that the ability to drive dopamine release may be critical for mood enhancement. Further, in a Phase 1 trial completed by its originator, ALTO-203 acutely increased subjective positive emotions by levels equivalent to or greater than modafinil, an U.S. Food and Drug Administration, or FDA, approved drug acting through dopamine release. The approach to treating depression through a dopamine-enhancing treatment, like modafinil or armodafinil, has been successful in third-party clinical trials in MDD and BPD.

*Previously Completed ALTO-203 Phase 1 Study in Healthy Volunteers*

ALTO-203 was previously studied in a Phase 1 study and demonstrated significant acute benefits on a scale of subjective positive emotion, compared to placebo. The magnitude of this effect was shown to be equivalent to, or better than modafinil, an active comparator with demonstrated antidepressant activity in clinical trials.

***ALTO-101***

*Overview*

ALTO-101 is an investigational brain-penetrant phosphodiesterase 4, or PDE4, inhibitor that we are developing in a novel transdermal formulation for the treatment of Cognitive Impairment Associated with Schizophrenia, or CIAS. Through this unique formulation, ALTO-101 is designed to retain the desired brain effects shown with the oral formulation and avoid tolerability challenges and adverse effects known to be associated with PDE4 inhibitors. In our completed Phase 1 trial, we demonstrated robust effects of ALTO-101 on cognitive processing, measured with EEG, and cognitive test performance. We are currently evaluating ALTO-101 in a Phase 2 POC trial, which consists of a cross-over, double-blind, placebo-controlled, dose-escalating treatment and we expect to enroll approximately 70 adults with schizophrenia between the ages of 21 and 55. The primary endpoint in the study is the effect of ALTO-101 on theta band activity, the EEG measure shown to be best related to CIAS in replicated analyses of large schizophrenia datasets. Objective cognitive performance will also be evaluated. We expect to report topline data in the second half of 2025.

We have pending patent applications to protect the utilization of the product candidate in the indications for which we are developing it. We believe our patent applications for ALTO-101 will provide protection to at least 2044.

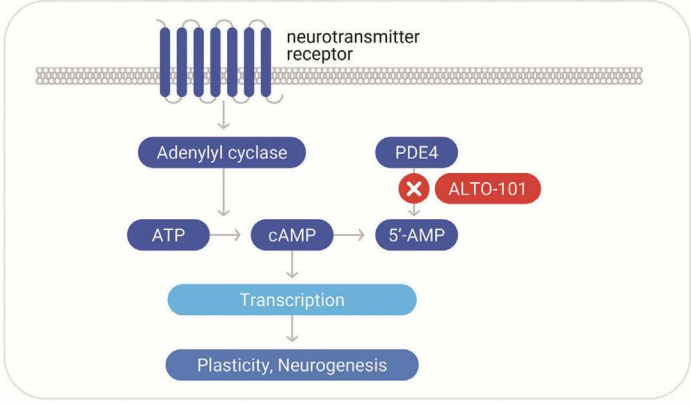
*CIAS Background*

Schizophrenia afflicts more than 2.8 million people in the United States alone. The hallmark symptoms of schizophrenia include hallucinations, delusions, irrational/illogical thoughts, and movement disorders. In addition to these positive symptoms, which are the target of all currently approved medications, approximately 90% of patients with schizophrenia also experience cognitive and/or negative symptoms. Cognitive symptoms include memory disturbances, inability to process information and make decisions, and trouble focusing or paying attention. Negative symptoms entail blunting of affect and are more akin to other affective disorders such as depression. Cognitive and negative symptoms of schizophrenia are also often more predictive of impairment in daily function than positive symptoms. Despite significant need for interventions to treat these aspects of schizophrenia, there are no currently approved treatments for the cognitive and negative symptoms.

*Background on ALTO-101*

ALTO-101 is a brain-penetrant small molecule that inhibits the PDE4 enzyme. PDE4 inhibition is relevant across numerous high-need therapeutic areas. However, available medications are non-brain penetrant with substantial tolerability and dosing limitations.

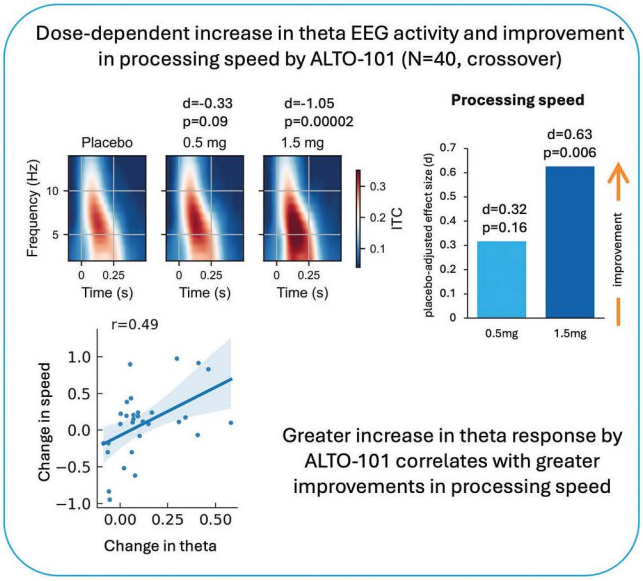
PDE4 normally acts to break down cyclic adenosine monophosphate, or cAMP, terminating its ability to drive downstream signaling. Post-mortem and genetic studies of patients with cognitive disorders, including schizophrenia, have demonstrated reduction in a key neuroplasticity-related second messenger signaling pathway involving cyclic adenosine monophosphate, or cAMP. This pathway has been extensively studied in humans and a wide range of preclinical models, with findings indicating that reduction in cAMP signaling has been observed to be associated with impaired cognition and mood, while increasing cAMP has been shown to rescue deficits in animal models of a variety of neuropsychiatric disorders. While several drugs that increase cAMP levels by inhibiting the breakdown of this second messenger are approved for non-CNS indications (e.g., psoriasis), none have yet been approved in the United States to treat neuropsychiatric disorders. By inhibiting PDE4, ALTO-101 is designed to elevate cAMP levels, which in the hippocampus has enhanced neuroplasticity and improved various forms of memory in preclinical models. ALTO-101 has demonstrated pro-cognitive effects in vivo at doses as low as five micrograms per kilogram. The figure below illustrates the potential mechanism of action of ALTO-101.

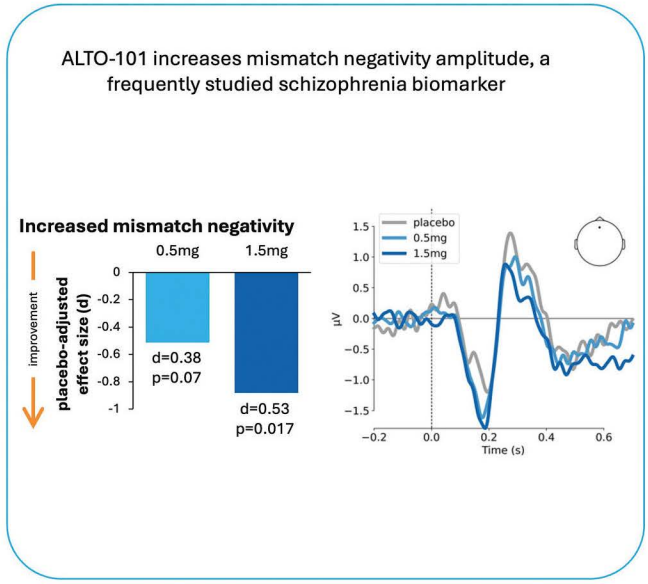



*Our Completed ALTO-101 Phase 1 Study in Healthy Subjects*

In order to understand the pharmacodynamic effects of ALTO-101 and neurocognitive outcomes relevant to CIAS, we completed a dose mapping trial in healthy subjects using our platform. Specifically, 40 individuals completed a three-condition cross-over design study, with each participant receiving single doses of placebo, 0.5mg, and 1.5mg of ALTO-101 orally at seven-day intervals. Key outcomes on EEG, event-related potentials, and neurocognitive task performance measures relevant to schizophrenia and other cognitive disorders were assessed. Compared to placebo, we observed significant effects in a dose response relationship for ALTO-101 on multiple measures including decreases in EEG resting theta power, which is known to be elevated in multiple cognitive and psychiatric disorders; increases in stimulus-driven gamma-band phase locking, which is known to be reduced in schizophrenia patients; and increases in mismatch negativity, which is known to be blunted in patients with schizophrenia. We also observed statistically significant, dose-dependent increases in information processing speed, a core cognitive domain important to multiple higher-level functions, as well as

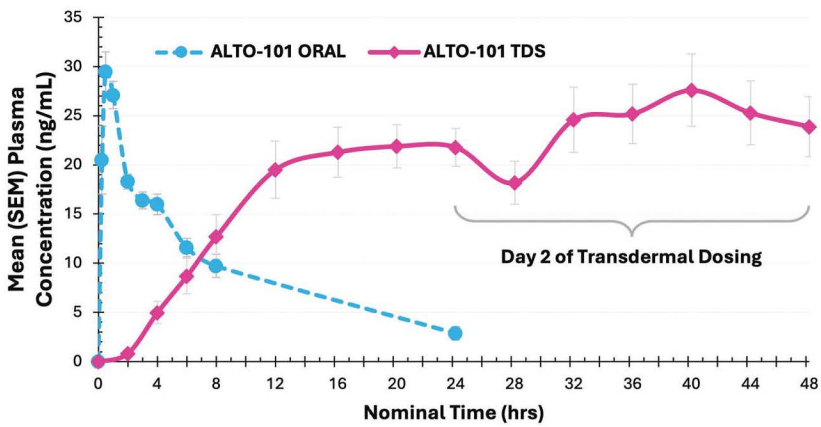
promising effects on a global cognition composite. We believe that these results support the potential utility of ALTO-101 as a pro-cognitive agent.




Higher doses of PDE4 inhibitors, broadly, have been associated with increased rates of nausea, which we believe is associated with peak concentrations in the brain after oral dosing. In our Phase 1 study, we likewise observed a dose-dependent increase in nausea (2.4% at 0.5mg and 28% at 1.5mg), dizziness (4.8% and 23.3%), and lightheadedness (2.4% and 14%), though only 2.3% of patients discontinued due to an adverse event. No serious treatment emergent adverse events, or TEAEs, were identified. The vast majority of these TEAEs occurred near Tmax, or the time it takes to reach peak drug concentration in the brain. Given the potency of ALTO-101, and our observation of its dose-response pharmacodynamic effects on brain biomarkers of cognition, we reformulated ALTO-101 to be delivered transdermally. The transdermal formulation, being developed in partnership with MedRx Co., Ltd., or MedRx, is designed to deliver a consistent and pharmacodynamically relevant dose while avoiding the peaks in blood concentration typical of immediate release oral drugs. See "—License and Other Agreements—License Agreement with MedRx" for further discussion.

We completed a Phase 1 trial in healthy subjects designed to evaluate the safety, tolerability, pharmacokinetics, and adhesion properties of a proprietary transdermal formulation of ALTO-101 compared to oral administration of ALTO-101 in healthy subjects. The transdermal formulation achieved similar maximum concentration as the oral formulation with a greater overall duration of exposure. The area under the curve was 62% and 170% higher on day 1 and day 2 respectively for the transdermal relative to oral administration (day 1 p=0.01; day 2 p<0.001). Further, the transdermal formulation was well-tolerated with no discontinuations. All adverse events reported in the study were mild in severity, and there were no reported serious adverse events. The transdermal formulation demonstrated favorable adhesion properties and there were no application site reactions that led to removal or intolerance. Taken together, our novel transdermal formulation of ALTO-101 exhibited greater systemic drug exposure than orally administered ALTO-101 while also demonstrating a reduction in typical class-related adverse events.



### *ALTO-202*

*Overview*

ALTO-202 is an investigational orally bioavailable antagonist of the GluN2B subunit of the NMDA receptor. NMDA receptors are receptors for glutamate, the major excitatory neurotransmitter in the brain, and its excessive release is associated with excitotoxicity-induced brain injury. This involvement of the glutamatergic system in depression is supported by the antidepressant effects of NMDA receptor antagonists, like ketamine and its enantiomer, esketamine. Given the evidence of antidepressant activity of NMDA receptor antagonists, and the drawbacks of those currently used, we plan to develop ALTO-202 in MDD as an oral GluN2B antagonist. We are currently in the process of planning the next phase of clinical development for ALTO-202.

*Background on ALTO-202*

Prior to our licensing of ALTO-202, it was evaluated by Merck and Cerecor across 10 clinical trials, including five Phase 1 safety and PK trials and two Phase 2 trials in MDD, a pilot study in treatment resistant depression, and two Phase 1b trials in patients with Parkinson's disease. Specifically, the originator conducted a 115-patient clinical trial using a sequential parallel comparison design, wherein patients received a sequential single dose regimen of 12 mg or 20 mg of ALTO-202 or placebo. The primary endpoint in the trial was the HDRS-6, using the average change across day two and day four post-dosing. ALTO-202 did not demonstrate statistically significant changes compared to placebo on the primary endpoint, but potentially clinically meaningful differences were observed on total HDRS score change at day two compared to placebo in a prespecified secondary analysis. Based on these results, we believe ALTO-202 may have potential rapid-onset antidepressant effects that could potentially be elucidated in a well-powered study. Across the trials, ALTO-202 was well tolerated with the most common adverse events being increased blood pressure, dizziness, somnolence, and paresthesia (numbness or tingling feeling). There were no treatment related serious adverse events observed in the prior studies of ALTO-202.

## License and Other Agreements

### *License Agreement with Stanford University*

In December 2019, we entered into an exclusive license agreement with equity, or the Stanford Agreement, with the Board of Trustees of the Leland Stanford Junior University, or Stanford, which was subsequently amended in May 2020 and December 2023.

Under the terms of the Stanford Agreement, we obtained a worldwide, royalty-bearing license, with the right to sublicense during the exclusive term only, under certain patent rights in five patent families relating to brain stimulation, electroencephalogram and functional MRI that we could use to guide treatment of psychiatry patients, or the Stanford Licensed Patents, and under certain technology relating to the inventions covered by the Stanford Licensed Patents, or Stanford Licensed Technology, to make, have made, use, sell, offer for sale and import licensed products for use in any indication. Our rights under the Stanford Licensed Patents are exclusive until December 2029, at which time it will become non-exclusive, and our rights under the Stanford Licensed Technology are non-exclusive. Some of the Stanford Licensed Patents are jointly owned by the United States Department of Veterans Affairs and/or the Board of Regents of the University of Texas System, or the UT Board, but all the Stanford Licensed Patents are exclusively managed by Stanford under invention management agreements between Stanford and those other institutions. Stanford retained the right for itself and all other non-profit research institutions to practice the Stanford Licensed Patents and use the Stanford Licensed Technology for any non-profit purpose, including sponsored research and collaborations. Additionally, the United States Government has the nonexclusive, nontransferable, irrevocable, royalty-free, paid-up right to practice or have practiced the Stanford Licensed Patents throughout the world by or on behalf of the United States Government and on behalf of other governments or organizations, and requires us to manufacture the licensed product substantially in the United States.

As partial consideration to acquire these license rights, we paid Stanford an upfront fee of $20,000 and reimbursed Stanford approximately $80,000 of prior patent prosecution expenses related to the licensed patents. Additionally, we are required to pay a low five-digit annual license maintenance fee beginning on each anniversary of the effective date through the term of the Stanford Agreement. We also issued an aggregate of 104,348 shares of our common stock to Stanford, the UT Board and five inventors, including Amit Etkin, M.D., Ph.D., our Chief Executive Officer. We additionally granted to Stanford a right to participate in subsequent private financings of our equity securities, pursuant to which Stanford has purchased an aggregate of 627,189 shares of our Series Seed and Series A convertible preferred stock. This purchase right terminated upon the closing of the IPO.

We are required to diligently develop, manufacture and offer to sell licensed products and to diligently develop markets for licensed products, in addition to meeting certain specified development and commercial diligence milestones. We do not owe any milestone payments to Stanford in connection with our development and commercialization of products or services covered by the Stanford Licensed Patents, however beginning with our first commercial sale of the licensed products, we owe Stanford royalties on aggregate annual net sales of all licensed products by us, our affiliates or sublicensees at a very low single digit percentage. We are also required to pay Stanford mid-teen to low-mid double digit percentages of any sublicensing consideration that we receive from third parties to whom we sublicense rights under the Stanford Licensed Patents, depending on the timing of entry into the applicable sublicense.

Unless terminated earlier, the Stanford Agreement will expire upon the expiration of the last Stanford Licensed Patent. Stanford has the right to terminate the Stanford Agreement on thirty days' written notice upon our uncured material breach of the Stanford Agreement, including failure to achieve the specified diligence milestones by the specified dates, as well as for certain other specified breaches. We have the right to terminate the Stanford Agreement for any reason upon specified prior written notice to Stanford.

***License Agreement with Sanofi***

In May 2021, we entered into a license agreement, or the Sanofi Agreement, with Sanofi, pursuant to which we obtained an exclusive, worldwide, royalty-bearing license, with the right to sublicense, under certain patent rights and know-how of Sanofi relating to a PDE4 inhibitor compound, now known as ALTO-101, to use, have used, develop, have developed, manufacture, have manufactured, commercialize, have commercialized or otherwise exploit ALTO-101 and products incorporating ALTO-101, or the Sanofi Licensed Products, for all human therapeutic, prophylactic and diagnostic uses. We also obtained a non-exclusive, worldwide license to use certain other specified know-how licensed to Sanofi by a specified third party to exploit Sanofi Licensed Products solely with respect to Parkinson's disease. During a time period that ends at a specified point in late-stage clinical development for the first Sanofi Licensed Product, Sanofi retains a limited right of first negotiation to negotiate to obtain from us, on an indication-by-indication basis, exclusive worldwide rights to exploit such Sanofi Licensed Product in such indication. If we do not agree upon terms for such exclusive license with Sanofi within a specified negotiation period, we are free to continue the development and commercialization of the Sanofi Licensed Product ourselves or via the grant of rights to any third party, subject to certain specified limitations on the grant of such rights, and the reinstatement of Sanofi's right of first negotiation after a specified period.

We are required to use commercially reasonable efforts to develop Sanofi Licensed Products and to obtain regulatory approval for Sanofi Licensed Products in at least one indication in each of the United States, a major European country, the United Kingdom and Japan or China, and to commercialize any Sanofi Licensed Product for which we obtain regulatory approval. We paid Sanofi an upfront fee of $0.5 million upon the entry into the Sanofi Agreement, and will be required to pay Sanofi up to an aggregate amount in the low-mid double digit millions upon the achievement of certain one-time development and regulatory approval milestones for the first Sanofi Licensed Product to achieve the specified milestone events. In addition, if we grant sublicenses under the patents and know how licensed to us under the Sanofi Agreement, we are required to pay sublicense revenue to Sanofi at tiered percentages ranging from low-mid double-digit percentages down to the very low double-digit percentages, reducing based on the time of entry into the applicable sublicense agreement.

If we achieve regulatory approval for one or more Sanofi Licensed Products, we will owe Sanofi certain commercial milestone payments for the achievement of specified levels of aggregate, annual worldwide net sales of all Sanofi Licensed Products, up to an aggregate amount of $102.0 million for all Sanofi Licensed Products. Beginning with our first commercial sale of a Sanofi Licensed Product, we will also be required to pay Sanofi a tiered royalty on aggregate, annual, worldwide net sales of Sanofi Licensed Products at percentages ranging from the mid-to-high single digits, subject to certain customary reductions that are applicable on a product-by-product and country-by-country basis, and a customary overall royalty floor. Royalties are payable, on an aggregate basis for all licensed products and all countries, with the royalty term commencing on a Sanofi Licensed Product-by-Sanofi Licensed Product and country-by-country basis on the first commercial sale of a Sanofi Licensed Product in such country, until the latest to occur of (a) expiration of the last valid claim of either a licensed patent or certain patents filed by us after the effective date of the Sanofi Agreement that claim the know-how licensed to us by Sanofi, (b) the expiration of any regulatory exclusivity for such Sanofi Licensed Products in such country, and (c) the tenth anniversary of the first commercial sale of such Sanofi Licensed Product in such country, or the Sanofi Royalty Term. The patents licensed from Sanofi are due to expire in 2033, without taking into account any possible patent term adjustment or extension or terminal disclaimers, and assuming payment of all appropriate maintenance, renewal, and fees. Please refer to the section titled "—Intellectual Property—Product Candidate Patent Portfolio" for details of certain patent terms.

In addition, if we use specified know-how licensed to Sanofi by the specified third party to exploit the Sanofi Licensed Products for Parkinson's disease, we will pay an additional premium at a mid-single digit percentage on all fees, milestone payments and royalties payable by us to Sanofi under the Sanofi Agreement, which premium will be payable by Sanofi directly to the specified third party.

Unless terminated earlier, the Sanofi Agreement will expire with respect to each licensed product, on a country-by-country basis, upon the expiration of the Sanofi Royalty Term, and with respect to the agreement in its entirety upon the expiry of the Sanofi Royalty Term for the last licensed product for which there has been a first commercial sale. Either we or Sanofi may terminate the Sanofi Agreement upon 60 days' prior written notice for the uncured material breach of the Sanofi Agreement by the other party. Sanofi also has the right to terminate the Sanofi Agreement for our insolvency or if we bring or otherwise participate in a patent challenge against any licensed patents. We may terminate the Sanofi Agreement for any reason upon specified prior written notice to Sanofi.

***License Agreement with Cerecor***

In May 2021, we entered into a patent and know-how license agreement, or the Cerecor Agreement, with Cerecor Inc. (n/k/a Avalo Therapeutics, Inc.), or Cerecor, pursuant to which we obtained an exclusive worldwide, royalty-bearing license, with the right to sublicense, under certain patent rights and know-how owned or controlled by Cerecor relating to an NR2B inhibitor compound now known as ALTO-202, including certain rights licensed to Cerecor by Essex Chemie AG, or Merck, to research, develop, make, have made, use, import, offer for sale and sell ALTO-202 and products incorporating ALTO-202, or Cerecor Licensed Products, for the prevention, diagnosis and/or treatment of all diseases in humans. Merck and its affiliates retained a co-exclusive, worldwide right under Merck's patent rights and know-how sublicensed to us by Cerecor to research, make, have made, use and import ALTO-202 and Cerecor Licensed Products solely for non-human, non-commercial purposes, and we received a non-exclusive worldwide, royalty-bearing license, with the right to sublicense, under certain patent rights covering improvements made by Merck through its exercise of such retained right. We are required to use commercially reasonable efforts to develop and commercialize at least one Cerecor Licensed Product in the licensed field in the United States, a major European country or Japan, whether ourselves or through an affiliate or licensee.

As partial consideration for the licenses granted by Cerecor, we paid Cerecor an upfront fee of $0.5 million. We will be required to pay Cerecor or Merck, depending on the specific milestone as set forth in the Cerecor Agreement, up to an aggregate of $59.1 million per Cerecor Licensed Product if we achieve certain development, regulatory approval and first commercial sale milestones for such Cerecor Licensed Product in up to a specified number of indications. If we successfully commercialize Cerecor Licensed Products, we will also be required to pay to Merck sales milestones totaling up to $15.0 million for all Cerecor Licensed Products, for the achievement of certain specified levels of worldwide annual aggregate net sales of all Cerecor Licensed Products. Beginning on the date of our first commercial sale of a Cerecor Licensed Product, on a Cerecor Licensed Product-by-Cerecor Licensed Product and country-by-country basis, we will also be obligated to pay Merck and Cerecor tiered royalties on aggregate annual worldwide net sales of such Cerecor Licensed Product at percentages in the high single digits in the aggregate, until the later of (a) the expiration of the last valid claim within the licensed patents covering such Cerecor Licensed Product in such country and (b) 10 years after the first commercial sale of such Cerecor Licensed Product in such country, or the Cerecor Royalty Term. The latest-expiring patents licensed from Cerecor are due to expire in 2040, without taking into account any possible patent term adjustment or extension or terminal disclaimers, and assuming payment of all appropriate maintenance, renewal, and fees. Please refer to the section titled "—Intellectual Property—Product Candidate Patent Portfolio" for details of certain patent terms. If we develop and commercialize a companion diagnostic as a standalone product in connection with a Cerecor Licensed Product, we will be required to make a one-time milestone payment to Cerecor upon the achievement of a specified level of net sales of such companion diagnostic product, at an amount in the very low single digit millions.

The Cerecor Agreement will remain in force, unless earlier terminated, until the expiration of the Cerecor Royalty Term. Either we or Cerecor may terminate the Cerecor Agreement upon 60 days' prior written notice for an uncured material breach of the Cerecor Agreement by the other party, or in the case of an insolvency event of the other party. We may terminate the agreement for any reason upon specified prior written notice to Cerecor.

***Teva Asset Purchase Agreement***

In October 2021, we entered into an asset purchase agreement, or the Teva Agreement, with Teva Pharmaceutical Industries, Ltd. and its affiliate Cephalon, Inc., or, together Teva, pursuant to which we acquired patents, know-how and other rights to ALTO-203 and a specified related compound, or Teva Acquired Compounds, and we assumed all post-acquisition liabilities related thereto. Pursuant to the Teva Agreement, we are required to use commercially reasonable

efforts to research, register, manufacture, develop, and commercialize the acquired assets, including exploiting products that incorporate a Teva Acquired Compound, or Teva Products.

As partial consideration for the acquisition of these rights, we paid Teva an upfront fee of $0.5 million. For the first Teva Product that we develop pursuant to the Teva Agreement, we are required to pay Teva up to an aggregate of $27.0 million upon the achievement of certain development and regulatory approval milestones ($0.5 million of which was paid to Teva in connection with the initiation of our Phase 2 POC trial evaluating ALTO-203), and up to $35.0 million in the aggregate for the achievement of certain tiered sales milestones for such Teva Product. In addition, if we successfully achieve regulatory approval, then beginning with first commercial sale, on a Teva Product-by-Teva Product and country-by-country basis, we will be required pay Teva tiered royalties on worldwide annual net sales of Teva Products at percentages ranging from the mid-single-digit to ten percent, until the latest to occur of (a) expiration of the last valid claim of an acquired patent covering the composition of matter, or use or formulation of the composition of matter of a Teva Acquired Compound incorporated in or comprising such Teva Product in such country, (b) the expiration of new chemical entity data and/or market exclusivity for such Teva Product in such country and (c) the 10th anniversary of the date of first commercial sale of such Teva Product in such country. The patents acquired from Teva covering ALTO-203 are due to expire in 2027, without taking into account any possible patent term adjustment or extension or terminal disclaimers, assuming payment of all appropriate maintenance, renewal, and fees, and unless the patents are invalidated earlier in a patent challenge. Please refer to the section titled "—Intellectual Property—Product Candidate Patent Portfolio" for details of certain patent terms.

***Palisade Asset Purchase Agreement***

In October 2021, we entered into an asset transfer agreement, or the Palisade Agreement, with Palisade to pursuant to which we acquired all patent, know-how and other rights to ALTO-100.

As partial consideration for the acquisition of these rights, we paid Palisade an upfront fee of $0.5 million. In addition, we will be required to pay Palisade up to an aggregate of $4.5 million upon the achievement of certain development and regulatory approval milestones for ALTO-100 (or a product containing ALTO-100 or otherwise derived from the acquired assets), or Palisade Acquired Products. If we sell or grant to a third party a license to the patents, know-how and other rights included in the acquired assets prior to the achievement of a specified clinical development milestone, we will be required to pay to Palisade a low-double digit percentage of any consideration received by us from such license or sale, provided that the maximum aggregate consideration we will be required to pay to Palisade under the Palisade Agreement, including the upfront payment and all potential milestones and transaction-related payments, will not exceed $5.0 million.

In connection with the transactions effected by the Palisade Agreement, Palisade also transferred and assigned to us all right, title, and interest in, to, and under an exclusive license agreement, or the Dow Agreement, between Dow Agrosciences LLC, or Dow, and Palisade (f/k/a Neuralstem, Inc.), dated as of December 1, 2016, as a result of which we obtained an exclusive, sublicensable license under certain patent rights of Dow to make, have made, use, and have used, certain compounds covered by such patent rights and to make, have made, offer for sale, sell, import, and have imported, products using such compounds, including Palisade Acquired Products, for the development, synthesis, and commercialization of such products as prescription human pharmaceutical in the United States. The patent rights licensed to us under the Dow Agreement cover an intermediate compound in the manufacturing process for ALTO-100.

Under the Dow Agreement, we are required to pay Dow an annual license maintenance fee that is customary for a license of this nature and not material to us. Additionally, we are required to pay Dow a single milestone payment that is customary for a license of this nature in the range of several million dollars upon the achievement of the first commercial sale of a product containing ALTO-100 (including any Palisade Acquired Product) in the United States. In addition, if we continue to manufacture ALTO-100 using a process that includes the manufacturing step covered by the patents included in the Dow Agreement, we will be required to pay Dow tiered royalties calculated as a percentage of any cash or non-cash consideration payable to us by our commercial partners that arise from net sales of products covered by the Dow patent rights, including Palisade Acquired Products, by such commercial partners, at percentages in the single digits. The licensed patent from Dow expires in 2029. Please refer to the section titled "—Intellectual Property—Product Candidate Patent Portfolio" for details of certain patent terms.

Unless earlier terminated, the Dow Agreement will expire upon the last to expire valid claim of the licensed patent rights in the United States. Either we or Dow may terminate the Dow Agreement for the uncured material breach of this Agreement by the other party following a specified notice period.

***License Agreement with MedRx***

In September 2023, we entered into a joint development and license agreement, or the MedRx Agreement, with MedRx Co., Ltd., or MedRx, pursuant to which we obtained an exclusive, sublicensable, worldwide license, with the right to sublicense, under certain patent rights and know-how of MedRx relating to transdermal drug delivery to develop (excluding any pre-clinical development), manufacture, and commercialize transdermally delivered pharmaceutical products comprising MedRx's transdermal patch technology and our ALTO-101, or MedRx Licensed Products, for all therapeutic, prophylactic, and diagnostic uses. We granted MedRx an exclusive, sublicensable, worldwide license under certain patent rights and know-how relating to ALTO-101 owned or controlled by us, including certain patents and know how licensed to us pursuant to the Sanofi Agreement, solely to conduct pre-clinical development and manufacturing of the MedRx Licensed Products for us in accordance with the MedRx Agreement and a separate manufacturing and supply agreement to be entered into between us and MedRx. During the term of the MedRx Agreement, we agreed that we will not, directly or indirectly, develop, manufacture, or commercialize any pharmaceutical product that is a transdermal patch formulation containing similar active pharmaceutical ingredients as ALTO-101 and that is used in the same field and labeled for the same indications as the MedRx Licensed Products, or MedRx Competitive Product. MedRx agreed that it will not, directly or indirectly, exploit any patch formulations of PDE4-inhibitor drugs for use within CNS disorders or exploit any MedRx Competitive Product, provided that if certain specified development or first commercial sale milestones are not achieved by certain specified dates, then MedRx has the right to cause the non-compete restrictions on both parties to lapse.

Under the MedRx Agreement, MedRx will be solely responsible for conducting all pre-clinical development of the MedRx Licensed Products to support IND and institutional review board filing, and we will be solely responsible for all other development (including non-clinical studies and clinical studies) necessary to obtain regulatory approval for the licensed products and subsequent commercialization of MedRx Licensed Products. We are obligated to use commercially reasonable efforts to commercialize the MedRx Licensed Products in each of the following countries in which we have obtained regulatory approval: the United States; at least two of Germany, Spain, France, Italy or the United Kingdom; and one of China or Japan.

Pursuant to the MedRx Agreement, we paid MedRx an upfront fee of $150,000. We are required to pay MedRx up to an aggregate of $11.0 million for the achievement of certain development and first commercial sale milestones for the first MedRx Licensed Product to achieve such milestones with respect to a first indication, and an additional milestone in the mid-single digit millions for each additional approved distinct indication for such first MedRx Licensed Product or a subsequent MedRx Licensed Product. In addition, we will be required to pay MedRx sales milestones based on the achievement of specified thresholds of aggregate annual worldwide net sales of all MedRx Licensed Products of up to $110.0 million in the aggregate, if all such sales thresholds are achieved. In April 2024, we achieved a milestone under the MedRx Agreement and paid MedRx $0.75 million in cash and issued MedRx 46,875 shares of our common stock.

Commencing on the first commercial sale of a MedRx Licensed Product, we will also be obligated to pay MedRx a mid-single digit royalty on annual, worldwide net sales of all MedRx Licensed Products, subject to certain customary reductions and a royalty floor. Royalties will be payable, on a MedRx Licensed Product-by-MedRx Licensed Product and country-by-country basis, until the latest to occur of (a) expiration of the last valid claim of certain specified patent rights covering such MedRx Licensed Products in such country, (b) the expiration of any regulatory exclusivity for such MedRx Licensed Product in such country, (c) the first approval of a specified generic product referencing such MedRx Licensed Product in such country, and (d) the tenth anniversary of the first commercial sale of such MedRx Licensed Product in such country, or the MedRx Royalty Term.

The MedRx Agreement will expire with respect to each MedRx Licensed Product, on a country-by-country basis, upon the expiration of the MedRx Royalty Term, and with respect to the entire MedRx Agreement upon the expiry of the last-to-expire MedRx Royalty Term for the last MedRx Licensed Product for which there has been a first commercial sale. Please refer to the section titled "Business—Intellectual Property—Product Candidate Patent Portfolio" for details of certain patent terms. Either we or MedRx may terminate the MedRx Agreement in its entirety or on a MedRx Licensed Product-by-MedRx Licensed Product basis upon an uncured material breach by the other party or in connection with an insolvency event of such party. In addition, if we or MedRx bring or otherwise participate in a patent challenge against any patents licensed by the other party, such other party may terminate the MedRx Agreement immediately. We have the right to terminate the MedRx Agreement in its entirety or on a MedRx Licensed Product-by-MedRx Licensed Product basis for any reason upon specified prior written notice to MedRx provided that the effective date of such termination will not be earlier than the completion date of a specified development event. We also have the right to terminate the MedRx Agreement with respect to a MedRx Licensed Product immediately upon our reasonable determination of a material safety issue with respect to such MedRx Licensed Product.

### *The Wellcome Trust Limited Convertible Grant Agreement*

In July 2024, we entered into a convertible loan agreement, or the Convertible Grant Agreement, with The Wellcome Trust Limited, or Wellcome. The Convertible Grant Agreement provides for an unsecured convertible loan, or the Convertible Loan, from Wellcome of up to approximately $11.7 million, payable in six tranches, $1.3 million of which was funded upon the execution of the Convertible Grant Agreement, and the remainder of which will be funded upon draw down of the remaining initiation payment or the completion of certain milestones as set forth in the Convertible Grant Agreement, subject to certain conditions. As of January 2025, we achieved a milestone under the Convertible Grant Agreement giving us the right to draw down a total of $3.8 million which represents the milestone and the remaining portion of the initiation payment.

We may use proceeds from the Convertible Loan solely to advance development of ALTO-100 in bipolar depression. In addition, if we do not exploit or develop ALTO-100 (other than for safety or efficacy concerns) within a specified period following the completion of our Phase 2b clinical trial evaluating ALTO-100 in patients with bipolar depression, the Convertible Grant Agreement provides Wellcome with a limited right to exploit ALTO-100, solely in bipolar depression, subject to a revenue share between Wellcome and us of any proceeds arising from Wellcome's exploitation. Outstanding amounts under the Convertible Loan accrue interest at an annual rate equal to the Sterling Overnight Index Rate plus 2%, subject to potential adjustment if such interest rate equals or exceeds 9% at any time. At any time after the second anniversary of the effective date of the Convertible Grant Agreement or in connection with an event of default, Wellcome has the right, at its election, to convert some or all of the Convertible Loan into shares of our common stock at a price per share equal to a 20% discount to the thirty-day volume-weighted average price of Common Stock on the New York Stock Exchange at the date of such conversion. The Convertible Grant Agreement provides that in no event shall the aggregate number of shares of our common stock issued pursuant to conversion of the Convertible Loan exceed 5,363,326, which is equal to 19.9% of the number of shares of our common stock outstanding as of the date of the Convertible Grant Agreement. At any time after the fifth anniversary of the date of the Convertible Grant Agreement or in connection with an event of default, Wellcome may require repayment of the Convertible Loan in full, together with accrued interest, to the extent not converted as described above.

## Intellectual Property

### *Overview*

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, whether developed internally or licensed from our collaborators or other third parties. 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, in part, on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of precision psychiatry and neuropsychiatric drug development; however, trade secrets are difficult to protect and provide us with only limited protection. 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 maintain our licenses to use intellectual property owned by third parties; and to defend and enforce our proprietary rights, including any patents that we own or may obtain in the future. Intellectual property rights may not address all potential threats to our competitive advantage.

As of December 31, 2024, we owned, co-owned, or have an exclusive license to approximately 137 patents and pending patent applications in the United States and foreign jurisdictions, including 22 issued U.S. patents and 45 issued foreign patents, with expected expiry dates between 2026 and 2044, without taking into account potentially available patent term adjustments or extensions in the United States and other countries, and assuming payment of all appropriate maintenance, renewal, and annuity fees.

### *Product Candidate Patent Portfolio*

As of December 31, 2024, we owned, co-owned, or have an exclusive license to approximately 110 patents and pending patent applications in the United States and foreign jurisdictions relating to our product candidates, including 13 issued U.S. patents and 37 issued foreign patents. Patents and patent applications directed to our most advanced programs are summarized below.

*ALTO-100*

With respect to ALTO-100, as of December 31, 2024, we owned three issued U.S. patents, 18 issued foreign patents, 12 pending U.S. patent applications, 10 pending foreign applications, and one pending international application with claims directed to composition of matter, method of manufacturing, and method of treating depression. The patents covering the method of manufacturing ALTO-100 are expected to expire in 2030. We in-license one patent from Dow directed to certain intermediate compounds useful in the manufacturing ALTO-100, which patent is expected to expire in 2029. Any patents covering the method of treating depression that may issue from such pending patent applications are expected to expire in 2042 or 2043, in each case, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. Our foreign patents and pending patent applications are filed in jurisdictions including Australia, Brazil, Canada, China, Israel, India, Japan, South Korea, Mexico, Philippines, Singapore, Hong Kong, Czech Republic, Germany, Spain, France, United Kingdom, Ireland, and Italy.

*ALTO-300*

With respect to ALTO-300, as of December 31, 2024, we owned three U.S. pending patent applications and one pending international application with claims directed to a method of treating depression in patients with certain EEG measurements. Any patents that issue from such pending patent applications are expected to expire in 2044, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees.

*ALTO-101*

With respect to ALTO-101, as of December 31, 2024, we owned seven U.S. pending patent applications and one pending international application with claims directed to method of treatment of neuropsychiatric disorders. Any patents that issue from these applications would be expected to expire in 2044 or 2045, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. We also exclusively in-license from Sanofi one issued U.S. patent and three issued foreign patents in Germany, France, and United Kingdom, which are expected to expire in 2033, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. Additionally, we exclusively in-license from MedRx one issued U.S. patent, one granted European patent, and two issued foreign patents in Japan and China, as well as two pending U.S. patent applications. The issued U.S. and foreign patents that are in-licensed from MedRx are expected to expire in 2034, and any patent issued from the pending patent application is expected to expire in 2034, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. We also co-own one pending international patent application with MedRx that is directed to an ALTO-101 formulation, which is expected to expire in 2044, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees.

*ALTO-203*

With respect to ALTO-203, as of December 31, 2024, we owned three issued U.S. patents with claims directed to composition of matter and method of treatment for cognition/cognitive disorders. These patents are expected to expire in 2027, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. In addition, we own two U.S. applications and one international application with claims directed to a method of treating a psychiatric or neurological disorder in a patient who has anhedonia with ALTO-203. These patents are expected to expire in 2044, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees.

*ALTO-202*

With respect to ALTO-202, as of December 31, 2024, we in-licensed from Cerecor one issued U.S. patent (owned by Merck and licensed to Cerecor) with claims directed to the composition of matter (ALTO-202 compound), which is expected to expire in 2026. We also in-licensed from Cerecor (co-owned with Merck) three issued U.S. patents and one pending U.S. application, and nine foreign issued patents or pending applications in Australia, Canada, China, Germany, Spain, France, India, United Kingdom, and Italy, with claims directed to composition of matter (polymorphic forms of

ALTO-202). These patents are expected to expire in 2035, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. Lastly, we in-licensed from Cerecor one pending U.S. application, with claims directed to a method of treatment. Any patents that issue from this application are expected to expire in 2040, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees.

***Precision Psychiatry Platform Patent Portfolio***

With respect to our Platform, as of December 31, 2024, we owned one pending U.S. patent application with claims directed to the method of identifying patient subtypes which relates to one aspect of our Platform. Any patent that issues from this application is expected to expire in 2040, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. We also exclusively in-license from Stanford five issued U.S. patents and one U.S. pending patent application with claims directed to machine learning techniques for identifying treatable patient populations. The issued patents are expected to expire between 2037 and 2040, and any patents that issue from the pending patent application are expected to expire in 2039, without taking into account any possible patent term adjustment or extensions or terminal disclaimers and assuming payment of all appropriate maintenance, renewal, and annuity fees. These Stanford patents may be relevant to future iterations of our Platform.

***Trademarks***

We also protect our brands, including through the procurement of trademark registrations. As of December 31, 2024, we owned U.S. trademark registrations for our house mark ALTO NEUROSCIENCE and our Brain logo.

***Intellectual Property Protection***

We continue to assess the extent to which we may seek additional patent protection for aspects of our product candidates. 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, or USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. Moreover, in the context of approved products, there may be additional exclusivity for the patents covering such approved products. 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 extended and only those patents with claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Patent term extension is available only for the first approved use of the drug, and thus, no extension is available if a product is approved for a subsequent use. Moreover, a patent can only be extended 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 other technologies. 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 early 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 Office. 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 we in-license, or patents that issue from our owned patent applications, 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. For more information regarding the risks related to our intellectual property, see the section titled "Risk Factors—Risks Related to Collaborations, Intellectual Property, and Related Agreements."

**Sales, Marketing, and Commercialization**

We do not currently have a commercial organization for the marketing, sales, and distribution of products. We intend to build our global commercialization capabilities internally over time, such that we are able to commercialize any product candidate for which we may obtain regulatory approval. We expect to manage sales, marketing, and distribution through internal resources and third-party relationships. In addition, we will opportunistically explore commercialization partnerships, particularly with entities that have strong capabilities in geographies outside the United States. As our current and future product candidates progress through clinical development, our commercial plans may change. Clinical data, the size of the development programs, the size of our target markets, the size of the requisite commercial infrastructure, and manufacturing needs may all influence our commercialization strategies.

**Manufacturing**

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We have engaged, and expect to continue to rely on, well-established third-party contract manufacturing organizations, or CMOs, to supply our product candidates for use in our preclinical studies and clinical trials. Because we rely on contract manufacturers, we employ personnel with extensive technical, manufacturing, analytical, and quality experience to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions. We believe our current manufacturers have the scale, systems, and experience to supply our currently planned clinical trials.

Additionally, we intend to rely on third-party CMOs for later-stage development and commercial manufacturing, if our product candidates receive marketing approval. As our lead product candidates advance through clinical development, we expect to enter into longer-term commercial supply agreements to fulfill and secure our production needs. While the drug substances used in our product candidates are manufactured by more than one supplier, the number of manufacturers is limited. In the event it is necessary or advisable to acquire supplies from an alternative supplier, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company. If we need to change manufacturers during the clinical or development stage for product candidates or after commercialization for our product candidates, if approved, the FDA and corresponding foreign regulatory agencies must approve these new manufacturers in advance, which will involve testing

and additional inspections to ensure compliance with FDA regulations and standards and may require significant lead times and delay.

To adequately meet our projected commercial manufacturing needs, our CMOs will need to scale-up production, or we will need to secure additional suppliers. Processes for producing drug substances and drug product for commercial supply are currently being developed, with the goal of achieving reliable, reproducible, and cost-effective production. We believe the drug substance and drug product processes for our current product candidates can be appropriately scaled.

**Competition**

The biopharmaceutical industry is characterized by the rapid innovation and intense competition. While we believe that our innovative precision psychiatry approach and pipeline of clinical assets provide us with competitive advantages, we face competition from multiple biopharmaceutical and biotechnology companies that are similarly working to develop therapeutics targeting neuropsychiatry and CNS disorders, as well as from academic institutions, governmental agencies, and public and private research institutions. Many of our potential competitors, either alone or with collaboration partners, have significantly greater financial 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 we are in achieving regulatory approvals and commercializing their products. 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. In particular we are developing our product candidates in the areas of major depressive disorder, bipolar depression, and schizophrenia. Notable examples of companies with either approved therapies or product candidates in development in areas that may be competitive in our areas of focus are AbbVie Inc.; Axsome Therapeutics, Inc.; Neumora Therapeutics, Inc.; Neurocrine Biosciences, Inc.; and Xenon Pharmaceuticals, Inc., among others. We believe the key competitive factors affecting the success of our product candidates that we develop to address MDD, BPD, schizophrenia, and other CNS disorders, if approved, are likely to be efficacy, safety, convenience, price, the level of generic competition, and the availability of reimbursement from government and other third-party payors.

**Government Regulation**

Government authorities in the United States, at the federal, state and, local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, and export and import of drug products. We, along with any third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our products and product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

***U.S. Drug Development Process***

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. A new drug must be approved by the FDA through the New Drug Application, or the NDA, process before it may be legally marketed in the United States. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA's Good Laboratory Practice, or GLP, regulations and other applicable requirements;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board, or 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 Practices, or GCP, regulations to evaluate the safety and efficacy of the proposed drug for its intended use;
- preparation of and submission to the FDA of an NDA after completion of all pivotal trials;

- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice, or cGMP, regulations to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and a potential inspection of selected clinical investigation sites to assess compliance with GCP regulations; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Once a product candidate is identified for development, it enters the preclinical development stage. The preclinical developmental stage generally involves laboratory evaluations of chemistry, formulation, and stability, as well as studies to evaluate the product candidate's toxicity in animals, in an effort to support subsequent clinical testing. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for certain studies.

Prior to beginning the first clinical trial with a product candidate in the United States, the trial sponsor must submit the results of preclinical testing, together with manufacturing information and analytical data, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical trials, detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the trial includes an efficacy evaluation. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product candidate, chemistry, manufacturing, and controls information, and any available human data or literature to support the use of the product candidate. Some preclinical testing may continue even after the IND is submitted. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such case, the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. Clinical holds also may be imposed by the FDA at any time after initiation of clinical trials due to safety concerns about ongoing or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of one or more qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP regulations, which include, among other things, the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials must be conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection and exclusion criteria, and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and a separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

Furthermore, an independent IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the consent form that must be signed by each trial subject or his or her legal representative, monitor the study until completed, and otherwise comply with IRB regulations. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. In addition, some clinical trials also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. There are also requirements governing the reporting of ongoing clinical studies and clinical trial results to public registries, including clinicaltrials.gov.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, excretion, and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and appropriate dosage.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide substantial evidence of efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide an adequate basis for product labeling.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These clinical trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval, and may be 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.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach alignment on the next phase of development.

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

***U.S. Review and Approval Process***

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees, unless a waiver or exemption applies.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality, and purity. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the filing date to complete a standard review of an NDA for a drug that is a new molecular entity. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted.

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

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP regulations.

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

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

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

***Regulation of Patch Formulations of Drugs as Combination Products in the United States***

Certain products are comprised of components, such as drug components and device components intended for drug delivery, which would normally be subject to different regulatory frameworks by the FDA and frequently regulated by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug-device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. We believe that any patch formulation of a product candidate that we develop would have a drug primary mode of action. A combination product with a primary mode of action attributable to the drug component generally would be reviewed and approved pursuant to the drug approval processes set forth in the FDCA. In reviewing the NDA for such a product, however, FDA reviewers would consult with their counterparts in the FDA's Center for Devices and Radiological Health to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability, and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality System Regulation, or QSR, applicable to medical devices.

***Expedited Development and Review Programs***

The FDA offers a number of programs intended to expedite the development or review of a marketing application for an investigational drug. For example, the Fast Track designation program is intended to expedite or facilitate the process for developing and reviewing product candidates that 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. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track

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

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the development and review processes, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate is designed to treat a serious condition, and if approved, would provide a significant improvement in safety or efficacy compared to available therapies for such disease or condition. The FDA will attempt to direct additional resources to the evaluation of a NDA designated for priority review in an effort to facilitate the review. For new-molecular-entity NDAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date, as compared to ten months for review of new-molecular-entity NDAs under its current PDUFA review goals.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefits, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of continued approval, the FDA will generally require the sponsor of a drug receiving accelerated approval to perform adequate and well-controlled confirmatory clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefits, and may require that such confirmatory trials be underway prior to granting accelerated approval. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory studies in a timely manner or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval 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.

***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, most 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. There also are continuing, annual program fees for any marketed products. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws and regulations. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP requirements and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of 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;
- fines, warning letters, or untitled letters;
- clinical holds on ongoing or planned clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labeling.

***Marketing Exclusivity***

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

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

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials.

***FDA Regulation of Companion Diagnostics and Clinical Decision Support Software***

If safe and effective use of a therapeutic depends on a device intended to identify patients most likely to benefit from the therapeutic, then the FDA generally will require approval or clearance of that device, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. Approval or clearance of the companion diagnostic will ensure that the companion diagnostic has been adequately evaluated and has adequate performance characteristics in the intended population. The review of companion diagnostics in conjunction with the review of our therapeutic product candidates will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health.

We currently anticipate that certain of our therapeutic product candidates will require us to develop and obtain FDA approval of a companion diagnostic for such therapeutic product candidates. This includes certain software applications, such as software that we are developing to identify biomarkers, that may also meet the definition of a medical device and be subject to FDA premarket authorization, depending on its classification and software function. FDA guidance adopts international principles established by the International Medical Device Regulators Forum for the clinical evaluation of software as a medical device, or SaMD, which refers to software that is intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.

The 21st Century Cures Act, or Cures Act, clarified the FDA's authority to regulate software functions as medical devices by amending the definition of "device" in the FDCA to exclude certain software functions, including clinical decision support software, or CDS, that meet certain criteria. Under the Cures Act and FDA CDS guidance, certain software functions are excluded from the FDCA's definition of "device" when they meet all the following criteria:

- not intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system;
- intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);
- intended for the purpose of supporting or providing recommendations to a healthcare professional about prevention, diagnosis, or treatment of a disease or condition; and
- intended for the purpose of enabling such healthcare professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such healthcare professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.

As a result, certain software functions may not be subject to FDA review pursuant to the Cures Act and related FDA CDS guidance. However, SaMD that does not meet the criteria set forth above generally will require marketing clearance or approval from the FDA prior to commercialization as described below.

In the United States, the laws and regulations governing the marketing of companion diagnostics are evolving, extremely complex, and in many instances, there are no significant regulatory or judicial interpretations of these laws and regulations. The FDCA defines a medical device to include any instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component part, or accessory, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals. The FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, the design and development, research, preclinical and clinical testing, manufacturing, safety, labeling, storage, recordkeeping, premarket clearance or approval, registration and listing, advertising and promotion, sales and distribution, export and import, and post-market surveillance of medical devices in the United States.

Unless an exemption applies, both hardware and SaMD companion diagnostics are regulated as medical devices by the FDA, and will require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are approval of an application for premarket approval, or PMA, and clearance of a premarket notification, or 510(k) clearance. There is also a third route to market for novel, low-to-moderate risk devices, called the *de novo* classification pathway.

On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance, for novel product candidates, a companion diagnostic device and its corresponding drug candidate should be approved or 510(k)-cleared contemporaneously by the FDA for the use indicated in the labeling of the therapeutic product.

*PMA Pathway*

Companion diagnostics, including both hardware and SaMD, are regulated by the FDA as medical devices. The FDA categorizes medical devices into one of three classes—Class I, II, or III—based on the risks presented by the device and the regulatory controls necessary to provide a reasonable assurance of the device's safety and effectiveness. Class I includes devices with the lowest risk to the patient and are those for which safety and effectiveness can be assured by adherence to the FDA's General Controls for medical devices, which include compliance with the applicable portions of the QSR facility registration and product listing, reporting of adverse medical events, and truthful and non-misleading labeling, advertising, and promotional materials. Class II devices are subject to the FDA's General Controls, and special controls as deemed necessary by the FDA to ensure the safety and effectiveness of the device. Special controls are established by the FDA for a specific device type and often include specific labeling provisions, performance metrics, and other types of controls that mitigate risks of the device (usually incorrect results for an *in-vitro* diagnostic device, or IVD). Devices deemed by the FDA to pose the greatest risks, such as life sustaining, life supporting or some implantable devices, or devices that have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally marketed device, are placed in Class III, requiring approval of a PMA. Some pre-amendment devices are unclassified, but are subject to the FDA's premarket notification and clearance process in order to be commercially distributed.

Class III devices generally require PMA approval before they can be marketed. Obtaining PMA approval requires the submission of "valid scientific evidence" to the FDA to support a finding of a reasonable assurance of the safety and effectiveness of the device. A PMA must provide complete analytical and clinical performance data and also information about the device and its components regarding, among other things, device design, manufacturing and labeling. Following receipt of a PMA, the FDA determines whether the application is sufficiently complete to permit a substantive review. If the FDA accepts the application for review, it has 180 days under the FDCA to complete its review of a PMA, although in practice, FDA's review often takes significantly longer, and can take up to several years. An advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. The FDA may or may not accept the panel's recommendation. As part of the FDA's review of a PMA, the FDA will typically inspect the manufacturer's facilities for compliance with QSR requirements, which impose requirements related to design controls, manufacturing controls, documentation and other quality assurance procedures. The user fee costs and the length of FDA review time for obtaining PMA approval are significantly higher than for a 510(k) notification or a *de novo* classification.

The FDA will approve the new device for commercial distribution if it determines that the data and information in the PMA constitute valid scientific evidence and that there is reasonable assurance that the device is safe and effective for its intended use(s). The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution, and collection of long-term follow-up data from patients in the clinical study that supported PMA approval or requirements to conduct additional clinical studies post-approval. The FDA may condition PMA approval on some form of post-market surveillance when deemed necessary to protect the public health or to provide additional safety and efficacy data for the device in a larger population or for a longer period of use. In such cases, the manufacturer might be required to follow certain patient groups for a number of years and to make periodic reports to the FDA on the clinical status of those patients. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of the approval.

Certain changes to an approved device, such as changes in manufacturing facilities, methods, or quality control procedures, or changes in the design performance specifications, which affect the safety or effectiveness of the device, require submission of a PMA supplement. PMA supplements often require submission of the same type of information as a PMA, except that the supplement is limited to information needed to support any changes from the device covered by the original PMA and may not require as extensive clinical data or the convening of an advisory panel. Certain other changes to an approved device require the submission of a new PMA, such as when the design change causes a different intended use, mode of operation, and technical basis of operation, or when the design change is so significant that a new generation of the device will be developed, and the data that were submitted with the original PMA are not applicable for the change in demonstrating a reasonable assurance of safety and effectiveness.

*510(k) Notification Pathway*

To obtain 510(k) clearance, a manufacturer must submit a premarket notification demonstrating to the FDA's satisfaction that the proposed device, including both hardware and SaMD, is "substantially equivalent" to another legally marketed device that itself does not require PMA approval (a predicate device). A predicate device is a legally marketed device that is not subject to premarket approval, i.e., a device that was legally marketed prior to May 28, 1976 (pre-amendments device) and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I, or a device that was found substantially equivalent through the 510(k) process. The FDA's 510(k) clearance process usually takes from three to twelve months, but often takes longer. FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence. In addition, the FDA collects user fees for certain medical device submissions and annual fees and for medical device establishments.

If the FDA agrees that the device is substantially equivalent to a lawfully marketed predicate device, it will grant 510(k) clearance to authorize the device for commercialization. If the FDA determines that the device is "not substantially equivalent" to a previously cleared device, the device is automatically designated as a Class III device. The device sponsor must then fulfill more rigorous PMA requirements, or can request a risk-based classification determination for the device in accordance with the *de novo* process, which is a route to market for novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device, discussed below.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change or modification in its intended use, will require a new 510(k) clearance or, depending on the modification, PMA approval. The FDA requires each manufacturer to determine whether the proposed change requires submission of a 510(k) or a PMA in the first instance, but the FDA can review any such decision and disagree with a manufacturer's determination. Many minor modifications are accomplished by a "letter to file" in which the manufacturer documents the rationale for the change and why a new 510(k) is not required. However, if the FDA disagrees with a manufacturer's determination, the FDA can require the manufacturer to cease marketing and/or request the recall of the modified device until 510(k) marketing clearance or PMA approval is obtained. Also, in these circumstances, the manufacturer may be subject to significant regulatory fines or penalties.

If no legally marketed predicate can be identified for a new device to enable use of the 510(k) pathway, the device is automatically classified under the FDCA into Class III, which generally requires PMA approval. However, the FDA can reclassify or seek *de novo* classification for a device that meets the FDCA standards for a Class I or Class II device, permitting the device to be marketed without PMA approval. To grant such a reclassification, the FDA must determine that the FDCA's general controls alone, or general controls and special controls together, are sufficient to provide a reasonable assurance of the device's safety and effectiveness. The *de novo* classification route is generally less burdensome than the PMA approval process.

*De Novo Classification*

Medical device types, including both hardware and SaMD, that the FDA has not previously classified as Class I, II or III are automatically classified under the FDCA into Class III regardless of the level of risk they pose. The Food and Drug Administration Modernization Act of 1997 established a route to market for low to moderate risk medical devices that are automatically placed into Class III due to the absence of a predicate device, called the "Request for Evaluation of Automatic Class III Designation," or the *de novo* classification procedure. This procedure allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents low or moderate risk, rather than requiring the submission and approval of a PMA application. Prior to the enactment of the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, a medical device could be eligible for de novo classification only if the manufacturer first submitted a 510(k) premarket notification and received a determination from the FDA that the device was not substantially equivalent to a legally marketed predicate device. FDASIA streamlined the *de novo* classification pathway by permitting manufacturers to request *de novo* classification directly without first submitting a 510(k) premarket notification to the FDA and receiving a not substantially equivalent determination. If the manufacturer seeks reclassification into Class II, the manufacturer must include a draft proposal for special controls that are necessary to provide a reasonable assurance of the safety and effectiveness of the medical device. In addition, the FDA may reject the request if it identifies a legally marketed predicate device that would be appropriate for a 510(k) notification, determines that the device is not low to moderate risk, or that general controls would be inadequate to control the risks and special controls cannot be developed. After a device receives *de novo* classification, any modification that could significantly affect its safety or efficacy, or that would constitute a major change or modification in its intended use, will require a new 510(k) clearance or, depending on the modification, another *de novo* request or even PMA approval.

*Investigational Device Exemption Process*

Clinical trials are almost always required to support a PMA and are sometimes required to support a 510(k) submission. All clinical investigations of investigational devices to determine safety and effectiveness must be conducted in accordance with the FDA's investigational device exemption, or IDE, regulations which govern investigational device labeling, prohibit promotion of the investigational device, and specify an array of recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. If the device presents a "significant risk" to human health, the FDA requires the device sponsor to submit an IDE application to the FDA, which must become effective prior to commencing human clinical trials. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a patient and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health, or otherwise presents a potential for serious risk to a subject. An IDE application must be supported by appropriate data, such as animal and laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE will automatically become effective 30 days after receipt by the FDA, unless the FDA notifies the company that the investigation may not begin. If the FDA determines that there are deficiencies or other concerns with an IDE for which it requires modification, the FDA may permit a clinical trial to proceed under a conditional approval.

In addition, the study must be approved by, and conducted under the oversight of, an IRB for each clinical site. The IRB is responsible for the initial and continuing review of the IDE, and may pose additional requirements for the conduct of the study. If an IDE application is approved by the FDA and one or more IRBs, human clinical trials may begin at a specific number of investigational sites with a specific number of patients, as approved by the FDA. If the device presents a non-significant risk to the patient, a sponsor may begin the clinical trial after obtaining approval for the trial by one or more IRBs without separate approval from the FDA, but must still follow abbreviated IDE requirements, such as monitoring the investigation, ensuring that the investigators obtain informed consent, and labeling and record-keeping requirements. Acceptance of an IDE application for review does not guarantee that the FDA will allow the IDE to become effective and, if it does become effective, the FDA may or may not determine that the data derived from the trials support the safety and effectiveness of the device or warrant the continuation of clinical trials. An IDE supplement must be submitted to, and approved by, the FDA before a sponsor or investigator may make a change to the investigational plan that may affect its scientific soundness, study plan or the rights, safety or welfare of human subjects.

During a study, the sponsor is required to comply with the applicable FDA requirements, including, for example, trial monitoring, selecting clinical investigators and providing them with the investigational plan, ensuring IRB review, adverse event reporting, record keeping, and prohibitions on the promotion of investigational devices or on making safety or effectiveness claims for them. The clinical investigators in the clinical study are also subject to FDA regulations and must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of the investigational device, and comply with all reporting and recordkeeping requirements. Additionally, after a trial begins, we, the FDA or the IRB could suspend or terminate a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits.

*Expedited Development and Review Programs for Medical Devices*

Through recent federal legislation, the FDA has implemented a Breakthrough Devices Program, which is a voluntary program offering manufacturers of certain devices an opportunity to interact with the FDA more frequently and efficiently as they develop their products with the goal of expediting commercialization of such products to help patients have more timely access. The program is available to medical devices that meet certain eligibility criteria, including that the device provides more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, and constitutes a device (i) that represents a breakthrough technology, (ii) for which no approved or cleared alternatives exist, (iii) that offer significant advantages over existing approved or cleared alternatives, or (iv) the availability of which is in the best interest of patients. Devices granted Breakthrough Device designation are eligible to rely on certain features of the Breakthrough Device Program, including interactive and timely communications with FDA staff, use of post-market data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design and priority review of premarket submissions.

*Postmarket Regulation of Medical Devices*

After a device is cleared or approved by the FDA for marketing, numerous and pervasive regulatory requirements continue to apply. These include:

- establishment registration and device listing with the FDA;

- QSR requirements, which require manufacturers, including third-party manufacturers, to follow stringent design, testing, control, documentation and other quality assurance procedures during all aspects of the design and manufacturing process;
- labeling regulations and FDA prohibitions against the promotion of "off-label" uses of cleared or approved products;
- requirements related to promotional activities;
- clearance or approval of product modifications to 510(k)-cleared devices that could significantly affect safety or effectiveness or that would constitute a major change in intended use of cleared devices, or approval of certain modifications to PMA-approved devices;
- medical device reporting regulations, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur;
- correction, removal, and recall reporting regulations, which require that manufacturers report to the FDA field corrections and product recalls or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FDCA that may present a risk to health;
- The FDA's recall authority, whereby the agency can order device manufacturers to recall from the market a product that is in violation of governing laws and regulations; and
- post-market surveillance activities and regulations, which apply when deemed by the FDA to be necessary to protect the public health or to provide additional safety and effectiveness data for the device.

Device manufacturing processes subject to FDA oversight are required to comply with the applicable portions of the QSR, which cover the methods and the facilities and controls for the design, manufacture, testing, production, processes, controls, quality assurance, labeling, packaging, distribution, installation, and servicing of finished devices intended for human use. The QSR also requires, among other things, maintenance of a device master file, device history file, and complaint files. Manufacturers are subject to periodic scheduled or unscheduled inspections by the FDA. A failure to maintain compliance with the QSR requirements could result in the shut-down of, or restrictions on, manufacturing operations and the recall or seizure of products. In February 2024, the FDA issued the Quality Management System Regulation Final Rule to amend the QSR, incorporating by reference the international standard for medical device quality management systems set by the ISO, ISO 13485:2016. The rule will become effective on February 2, 2026. Until then, manufacturers are required to comply with the QSR. The discovery of previously unknown problems with products, including unanticipated adverse events or adverse events of increasing severity or frequency, whether resulting from the use of the device within the scope of its clearance or off-label by a physician in the practice of medicine, could result in restrictions on the device, including the removal of the product from the market or voluntary or mandatory device recalls.

The FDA has broad regulatory compliance and enforcement powers. If the FDA determines that a manufacturer has failed to comply with applicable regulatory requirements, it can take a variety of compliance or enforcement actions, including the following:

- issuance of warning letters, untitled letters, fines, injunctions, consent decrees, and civil penalties;
- requesting or requiring recalls, withdrawals, or administrative detention or seizure of our products;
- imposing operating restrictions or partial suspension or total shutdown of production;
- refusing or delaying requests for 510(k) marketing clearance or PMA approvals of new products or modified products;
- withdrawing 510(k) clearances or PMA approvals that have already been granted;
- refusal to grant export approvals for our products; or
- criminal prosecution.

***Healthcare Reform***

In the United States, there have been, and continue to be, legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate

post-approval activities, and affect the profitable sale of product candidates, and similar healthcare laws and regulations exist in the European Union, or EU, and other jurisdictions. Among policy makers and payors in the United States, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

By way of example, in March 2010, the Patient Protection and Affordable Care Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA, among other things, increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs; implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and political challenges and amendments to certain aspects of the ACA. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or the IRA, was signed into law, which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. It is unclear how other healthcare reform measures, if any, will impact our business

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024. Further, in August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect until 2032, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, heightened governmental scrutiny is likely to continue over the manner in which manufacturers set prices for their marketed products, which already has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Most recently, among other things, the IRA requires manufacturers of certain drugs that have been on the market for at least seven years to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA permits the Secretary of the Department of Health and Human Services, or HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs as implemented. Further, on February 14, 2023, HHS released a report outlining three new models for testing by the Center for Medicare and Medicaid Innovation which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.

Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in

reduced demand for our products once approved or additional pricing pressures. 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.

***Other U.S. Healthcare Laws and Compliance Requirements***

In the United States, our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, CMS, other divisions of HHS, (*e.g.*, the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our business practices, including our clinical research program and any future sales, marketing and scientific/educational grant programs may be required to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, transparency requirements, and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. In addition, 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. Rather, if "one purpose" of the remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to, among others, a federal healthcare program that the person knows or should know is for a medical or other item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws, including the federal False Claims Act, or FCA, impose significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit, any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs such as Medicare and Medicaid, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. In addition, a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA.

Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like 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.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, also imposes certain obligations, including mandatory contractual terms, with respect to

safeguarding the privacy and security of individually identifiable health information of covered entities subject to the rule, including health plans, healthcare clearinghouses and certain healthcare providers and their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information for or on their behalf, as well as their covered subcontractors.

Additionally, the federal Physician Payments Sunshine Act, or the Sunshine Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually to CMS certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states also govern the reporting of payments or other transfers of value, many which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

Also, many states have similar, and typically more prohibitive, fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, we may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***Coverage, Pricing, and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations.

The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective.

A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. In addition, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Further, obtaining reimbursement for our product may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of physicians. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

We may develop products that, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain biopharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other EU member states allow companies to fix their own prices for medicines, but monitor and control company profits. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

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, or HTA Regulation, was adopted. The HTA 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. The HTA Regulation entered into application on January 12, 2025 through a phased implementation based on the type of product (i.e. oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030) and is intended to harmonize the clinical benefit assessment of HTA across the EU and is intended to harmonize the clinical benefit assessment of HTA across the EU.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. The downward pressure on the rise in healthcare costs in general and pharmaceutical products in particular has become intense. As a result, in the EU, increasingly high barriers are being erected to the entry of new products. In the United States, the emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes has increased and we expect will continue to increase the pressure on product pricing. In addition, coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

***Foreign Government Regulation***

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries governing, among other things, clinical trials, marketing authorization, 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. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, promotion, and reimbursement vary greatly from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

***The Foreign Corrupt Practices Act***

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

***Additional Regulation***

In addition to the foregoing, state, federal, and foreign laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

***Data Privacy and Security***

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, including clinical trial data. Certain of these laws, regulations, and standards apply now to our operations, and additional such laws, regulations, and standards could in the future apply to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, and consumer protection laws and regulations, govern the collection, use, disclosure, and protection of health-related and other personal information. Further, to the extent we collect personal data from individuals outside of the United States, through clinical trials or otherwise, we could be subject to foreign laws, such as the GDPR, which govern the privacy and security of personal data, including health-related data. Our use of artificial intelligence and machine learning may also be subject to evolving laws and regulations regarding security and privacy, as well as controlling for data bias and anti-discrimination. 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.

**Employees and Human Capital Resources**

As of December 31, 2024, we had 76 total employees, including 72 in the United States and four in Australia. Of our 76 employees, 18 hold Ph.D. and/or M.D. degrees and 58 were engaged in research and development. 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 continued ability to attract, retain, and motivate exceptional employees is vital to ensuring our long-term competitive advantage. Our employees are critical to our long-term success and are essential to helping us meet our goals. 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 and cash-based performance bonus awards.

**Corporate Information and Trademarks**

Alto Neuroscience, Inc. was incorporated under the laws of the State of Delaware in March 2019. Our principal executive office is located at 650 Castro Street, Suite 450, Mountain View, CA 94041. Our telephone number is (650) 200-0412. Our website address is www.altoneuroscience.com. Information contained in, or accessible through, our website does not constitute a part of, and is not incorporated into, this Annual Report.

The Alto Neuroscience logo, the name Alto Neuroscience, and other trademarks of Alto Neuroscience, Inc. appearing in this Annual Report are the property of Alto Neuroscience, Inc. Solely for convenience, trade names, trademarks, and service marks contained in this Annual Report may appear without the "®" or "™" symbols. Such references are not intended to indicate, in any way, that the respective owners will not assert, to the fullest extent possible under applicable law, their rights to those trade names, trademarks, and service marks.

**Additional Information**

Our Internet website address is www.altoneuroscience.com. On our website, we make available, free of charge, our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after the company electronically files such material with, or furnishes such material to, the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding us and other companies that file materials with the SEC electronically.

Also available on our website is information relating to our corporate governance and our board of directors, including our corporate governance guidelines; our code of business conduct (for our directors, officers and employees); and our board committee charters. We will provide any of the foregoing information without charge upon written request to our Corporate Secretary, 650 Castro Street, Suite 450, Mountain View, CA 94041.

## Item 1A. Risk Factors.

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report, including our consolidated financial statements and their related notes included elsewhere in this Annual Report and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" before making an investment decision. If any of the following risks actually occurs, our business, prospects, operating results, and financial condition could suffer materially, the trading price of our common stock could decline, and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial also may materially and adversely affect our business, prospects, operating results, and financial condition.*

### Summary of Selected Risk Factors Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are more fully described in this "Risk Factors" section, including the following:

- We are a clinical-stage biopharmaceutical company with a limited operating history and no history of commercializing products and have incurred substantial losses since our inception. We anticipate incurring substantial and increasing losses for the foreseeable future and may never achieve or maintain profitability.

- 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.

- 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.

- We rely heavily on the biomarker data gathered from our Platform. We currently anticipate that certain of our therapeutic product candidates will require us to develop and obtain FDA approval of a companion diagnostic for such therapeutic product candidates. We expect to initiate discussions with the FDA concerning the development of companion diagnostics at our end of Phase 2 meetings with respect to ALTO-100 and ALTO-300. If the FDA does not agree with our biomarker-based approach, or if we are unable to successfully develop and obtain regulatory approval for certain companion diagnostic tools needed to leverage our Platform, or experience significant delays in doing so, our business will be materially harmed.

- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us or any future collaboration partners from obtaining approvals for the commercialization of our product candidates, and additional time may be required to obtain marketing authorization for any of our product candidates that we develop as drug/device combination products.

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

- The successful commercialization of our product candidates, if approved, will depend in part on the extent to which governmental authorities and health 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.

- Our business depends on the success of our product candidates. If we are ultimately unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

- We rely on, and intend to continue to rely on, our internal clinical development expertise to conduct our current and future clinical trials, including internal teams and systems as well as external vendors and CROs. If our team is unable to execute according to our strategy, comply with regulatory requirements, or run trials effectively, our ability to obtain regulatory approval may be delayed and our business could be materially harmed.

- The terms of our Amended Loan Agreement and the Convertible Grant Agreement place restrictions on our operating and financial flexibility and may cause dilution to our stockholders. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business or result in further dilution to investors in our common stock.

- Competitive products may reduce or eliminate the commercial opportunity for our product candidates for our current or future indications. If our competitors develop technologies or product candidates more rapidly than we do, or their technologies are more effective or safer than ours, our ability to develop and successfully commercialize our current products may be adversely affected.

- We are dependent on the services of our management and other clinical and scientific personnel, including our internal clinical operations team, 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 Platform, technologies, and 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. Further, our issued composition of matter patents covering our pharmaceutical product candidates may expire at such a date that our patents may not prevent competitors from developing, making, and marketing a product that is identical to our product candidates after expiration of any applicable regulatory exclusivities. For example, our composition of matter patents covering ALTO-100 expired and patents covering its method of manufacturing are due to expire in 2030; our composition of matter patents in ALTO-202 (compound) expired (in foreign countries) and are due to expire in 2026 (in the United States), and our polymorph composition of matter patents in ALTO-202 are due to expire in 2035; and our composition of matter patents in ALTO-203 are due to expire in 2027, in all cases without taking into account patent term extensions or adjustments, and assuming payment of all applicable maintenance, renewal, and annuity fees.

- Our rights to develop and commercialize our product candidates, our Platform, or other technologies are subject, in large part, to the terms and conditions of licenses granted to us by others, such as Stanford, Sanofi, and MedRx. The terms of these licenses may be inadequate to protect our competitive position on products or product candidates for a sufficient amount of time. For example, our patent rights under the terms of our exclusive license agreement with Stanford are only exclusive until December 2029, at which time such rights will become nonexclusive, and our rights under certain technology relating to the inventions covered by such patents are nonexclusive. Further, if we fail to comply with our obligations in the 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.

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

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

**Risks Related to Our Limited Operating History, Financial Position, and Need for Capital**

***We are a clinical-stage biopharmaceutical company with a limited operating history and no history of commercializing products, which may make it difficult to evaluate our approach to the discovery and development of product candidates and the prospects for our future viability.***

We are a clinical-stage biopharmaceutical company with a limited operating history. We were formed in 2019 and our operations to date have been limited to organizing, staffing, and financing our company, in-licensing our technology, and conducting research and development activities, including developing our Platform, conducting clinical trials for our product candidates, and establishing our intellectual product portfolio. If we are successful in achieving regulatory approval for our product candidates, we will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Our approach to the discovery and development of product candidates based on our Platform is unproven, and we do not know whether we will be able to develop any product candidates that succeed in clinical development or products of commercial value. Moreover, as an organization, we have not yet demonstrated an ability to obtain regulatory approvals,

manufacture a commercial-scale product or arrange for a third party to do so on our behalf, conduct sales and marketing activities necessary for successful product commercialization, or generate revenues. We may encounter unforeseen expenses, difficulties, complications, delays, and other known or unknown factors in achieving our business objectives. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays, and difficulties frequently encountered by companies in clinical development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

***We have incurred substantial losses since our inception. We anticipate incurring substantial and increasing losses for the foreseeable future and may never achieve or maintain profitability.***

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date. As a result, we are not profitable, have incurred substantial losses in each period since our inception, and we expect to incur significant losses for the foreseeable future.

For the years ended December 31, 2024, and 2023, our net losses were approximately $61.4 million and $36.3 million, respectively. As of December 31, 2024, we had an accumulated deficit of approximately $138.4 million. Substantially all of our losses have resulted from expenses incurred in connection with the acquisition and development of our pipeline and Platform, research and development, and clinical trial costs, 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. We anticipate that our expenses will increase substantially if, and as, we:

- conduct further clinical trials for ALTO-100, ALTO-300, ALTO-101, ALTO-203, ALTO-202, and advance our preclinical programs into the clinic;
- 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 product candidates or any future product candidates;
- commercialize our current product candidates or any future product candidates, if approved;
- take steps toward our goal of being an integrated biopharmaceutical 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 regulatory approval for our product candidates due to macroeconomic conditions, geopolitical conflicts, or other global events; and
- incur additional costs, including legal, accounting, and other expenses, associated with operating as a public company.

We have no product candidates approved for commercial sale and have not generated any revenue from the sale of products. Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue, if any, unless and until we, either alone or with a collaborator, are able to obtain regulatory approval for, and successfully commercialize, one of our product candidates for our initial and potential additional indications, or any other product candidates we may develop.

Successful commercialization will require achievement of many key milestones, including demonstrating safety and efficacy in clinical trials, obtaining regulatory, including marketing approval for these product candidates, manufacturing, marketing, and selling those products for which we, or any of our future collaborators, may obtain regulatory approval, satisfying any post-marketing requirements, and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any further losses, or if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Additionally, our expenses could increase if we are required by the FDA or any comparable foreign regulatory authority to perform clinical trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates.

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 and our working capital. Our failure to become and remain profitable may depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings, or continue our operations. If we continue to suffer losses as we have in the past, you may not receive any return on your investment and may lose your entire investment.

***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.***

Our operations have consumed substantial amounts of cash since our inception. We expect to continue to spend substantial amounts of cash to conduct further research and development, preclinical studies, and clinical trials of our current and future product candidates, to seek regulatory approvals for our current product candidates, and to launch and commercialize any products if we receive regulatory approval.

As of December 31, 2024, we had $168.7 million of cash, cash equivalents and restricted cash. Based upon our current operating plan, we believe that our existing cash and cash equivalents as of the date of filing of this Quarterly Report, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. Our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and we will in any event require additional capital in order to complete clinical development of any of our current programs. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our programs and product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and future commercialization activities, if any. Our future capital requirements will depend on many factors, including:

- the scope, timing, progress, costs, and results of discovery, preclinical development, and clinical trials for our current or future product candidates;
- the number of clinical trials required for regulatory approval of our current or future product candidates;
- the costs, timing, and outcome of regulatory review of any of our current or future product candidates;
- the costs associated with acquiring or licensing additional product candidates, technologies, or assets, including the timing and amount of any milestones, royalties, or other payments due in connection with our acquisitions and licenses;
- the cost of manufacturing clinical and commercial supplies of our current or future product candidates;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the effectiveness of our Platform in identifying target patient populations and utilizing our approach to enrich our patient population in our clinical trials;

- our ability to maintain existing, and establish new, strategic collaborations or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty, or other payments due under any such agreement;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- expenses to attract, hire, and retain skilled personnel;
- the costs of operating as a public company;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payors;
- our ability to mitigate the impact of adverse macroeconomic conditions or other geopolitical events, the ongoing conflicts between Ukraine and Russia and in the Middle East, geopolitical tensions in China, inflation, fluctuating interest rates, tariffs, or other factors on our preclinical and clinical development or operations;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in business, products, and technologies.

We will require substantial additional capital to achieve our business objectives. Additional funds may not be available on a timely basis, on favorable terms or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. Market volatility resulting from adverse macroeconomic conditions or geopolitical events, including the ongoing conflicts between Ukraine and Russia and in the Middle East, geopolitical tensions in China, inflation, fluctuating interest rates, proposed tariffs, or other factors may further adversely impact our ability to access capital as and when needed. 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.

If we raise additional funds through future collaborations, licenses, and other similar arrangements, we may have to relinquish valuable rights to our future revenue streams or product candidates, or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we would be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***The obligations from our license and asset acquisition agreements may cause dilution to our stockholders, may be a drain on our cash resources, or may cause us to incur debt obligations to satisfy the payment obligations.***

Under the terms of certain of our license and acquisition agreements, the counterparties to such agreements are entitled to substantial contingent payments upon the occurrence of certain events. For example, under the terms of our license agreement with Sanofi, we will be required to pay Sanofi up to an aggregate amount in the low-mid double digit millions upon the achievement of certain one-time development and regulatory approval milestones with respect to ALTO-101, and, if regulatory approval is achieved, up to an aggregate amount of $102.0 million in commercial milestone payments and a tiered royalty on aggregate annual worldwide net sales at percentages ranging from the mid-to-high single digits. Under the terms of our license agreement with Cerecor, we will be required to pay Cerecor or Merck, depending on the milestone, up to an aggregate of $59.1 million if we achieve certain development, regulatory, and first commercial sale milestones for ALTO-202. If we successfully commercialize ALTO-202, we will be required to pay Merck sales milestones in an amount of up to $15.0 million. Beginning on the date of our first commercial sale of ALTO-202, we will also be obligated to pay Merck and Cerecor tiered royalties on aggregate annual worldwide net sales at percentages in the high single digits, in

addition to potential payments in respect of a companion diagnostic product. Pursuant to our asset purchase agreement with Teva, pursuant to which we acquired the rights to ALTO-203, we may be required to pay up to an aggregate of $27.0 million upon the achievement of certain development and regulatory approval milestones ($0.5 million of which was paid to Teva in connection with the initiation of our Phase 2 POC trial evaluating ALTO-203), and up to $35.0 million for the achievement of certain tiered sales milestones, as well as tiered royalties on worldwide annual net sales at percentages ranging from the mid-single-digit to ten percent. Pursuant to our joint development and license agreement with MedRx, we are required to pay MedRx up to an aggregate of $11.0 million for the achievement of certain development and first commercial sale milestones for ALTO-101 with respect to a first indication, an additional milestone in the mid single digit millions for each additional approved distinct indication for ALTO-101, as well as sales milestones based on the achievement of specified levels of aggregate annual worldwide net sales of up to $110.0 million in the aggregate and a mid-single digit royalty on annual, worldwide net sales. In April 2024, we achieved a milestone under the MedRx Agreement and paid MedRx approximately $0.8 million in cash and issued MedRx 46,875 shares of our common stock. If we achieve certain development and regulatory approval milestones for a product that contains ALTO-100 or is otherwise derived from assets we acquired from Palisade we will be required to pay Palisade up to an aggregate of $4.5 million. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Contractual Obligations and Commitments" in this Annual Report for additional information regarding these agreements.

In order to satisfy our obligations to make these payments, if and when they are triggered, we may need to issue equity or convertible debt securities that may cause dilution to our stockholders, or we may use our existing cash and cash equivalents or incur debt obligations to satisfy the payment obligations in cash, which may adversely affect our financial position. In addition, these obligations may impede our ability to raise money in future public offerings of debt or equity securities or to obtain a third-party line of credit.

**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.***

All of our product candidates are in preclinical or clinical development and their risk of failure is high. In particular, our approach to utilizing our Platform to identify biomarkers and conducting clinical trials in patient populations expressing certain biomarkers has not been validated and may not prove to be successful. It is impossible to predict when or if any of our product candidates will receive regulatory approval. To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through lengthy, complex, and expensive clinical trials that our product candidates are safe and effective in patient populations identified by our Platform for the relevant indication. Preclinical and clinical testing can take many years to complete, and its outcome is inherently uncertain. There is typically a high rate of failure of product candidates proceeding through clinical trials, and failure can occur at any time during the preclinical study or clinical trial process, despite promising preclinical or clinical results. 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, in October 2024, we reported that our Phase 2b trial of ALTO-100 in patients with MDD did not meet its primary endpoint. 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. Certain of our product candidates were previously subject to all-comer population studies and were not progressed for further development or did not achieve statistically significant outcomes. For example, ALTO-100 demonstrated numerical improvements in MADRS scores but did not achieve statistically significant outcomes in a prior all-comer population study. There can be no assurance that our results to date for these product candidates in our biomarker-characterized patient populations will continue or that the results of our trials will continue to differ from the outcomes of prior all-comer studies. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates achieved promising results have nonetheless failed to obtain marketing approval of such product candidates. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful.

In addition, our approach of identifying biomarkers and conducting clinical trials in patient populations expressing those biomarkers is unique, unproven, and does not have significant precedent with the FDA and the FDA has, thus far, not affirmatively adopted our approach. Commencing any future clinical trials is subject to finalizing the trial protocol and submitting an IND to the FDA or similar application to initiate a clinical study to 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 preclinical studies or amend our protocols or impose stricter conditions on the commencement of clinical trials, which may lead to delays and increase the costs of our preclinical development programs. The FDA also has the authority to require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, could have a significant impact on our ability to obtain approval of any product candidates. Similar decisions may also be made by foreign regulatory authorities and have similar impact.

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 clinical trial sites and clinical trial teams to ensure the proper and timely conduct of our clinical trials, including the participant enrollment process, and we have limited influence over their performance. In addition, we may in the future enter into collaboration agreements pursuant to which our collaborator would be responsible for clinical development. We or our 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 marketing approval or commercialize our current and any future product candidates, including:

- regulators, such as the FDA or comparable foreign regulatory agencies, Institutional Review Boards, or IRBs, or ethics committees may impose additional requirements before permitting us to initiate a clinical trial, may not authorize 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 disagree as to the design or implementation of our clinical trials and 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 clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among trial sites;
- delays in identifying, recruiting, and training suitable clinical investigators;
- IRBs refusing to approve, suspending, or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes or amendments to the clinical trial protocol;
- clinical trial sites may deviate from the trial protocol or drop out of a trial;
- failure by any of our third-party contractors to perform in accordance with GCP requirements or applicable regulatory rules and guidelines in other countries;
- the number of participants required for clinical trials may be larger than we anticipate, we may experience difficulty in finding and enrolling sufficient qualified patients for our biomarker-guided trials, 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;
- subjects may fail to enroll or remain in our trials at the rate we expect, or fail to return for post-treatment follow-up, including subjects failing to remain in our trials due to movement;
- patients choosing an alternative product for the indications for which we are developing our product candidates, or participating in competing clinical trials;
- the cost of clinical trials may be greater than we anticipate;
- 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;
- we may experience difficulties in manufacturing, or fail to manufacture, sufficient quantities of our product candidates for use in clinical trials;

- we may experience delays in developing and validating our companion diagnostics to be used in a clinical trial, if applicable;
- subjects experiencing severe or serious unexpected drug-related adverse effects;
- reports from clinical testing conducted by other companies of other therapies in the same class of agents that could be considered similar to our product candidates may raise safety, tolerability, or efficacy concerns about our product candidates;
- we may lack adequate funding to initiate or continue one or more of our clinical trials;
- selection of clinical endpoints that require prolonged periods of clinical observation or extended analysis of the resulting data;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice, or cGMP, regulations or other applicable requirements, or cross-contaminations of product candidates in the manufacturing process;
- changes to our manufacturing processes may be necessary or desired;
- third-party clinical investigators may lose the licenses or permits necessary to perform our clinical trials and may fail to perform our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or other regulatory requirements;
- third-party contractors being unwilling or unable to satisfy their contractual obligations to us in a timely or accurate manner;
- third-party contractors could be debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; and
- 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.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations, and guidelines, and remain subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where such clinical trials are conducted. We could encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the FDA or comparable foreign regulatory authorities, or the Data Safety Monitoring Board, or the DSMB, for such trial. A suspension 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 trial protocols, adverse findings from inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities, 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. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to regulators or to IRBs for reexamination, which may impact the costs, timing, or successful completion of a clinical trial. For example, recently the FDA informed us of a partial clinical hold related to a limit on the exposure level of ALTO-101 in our ongoing Phase 2 POC trial, which we subsequently resolved by amending the dosing paradigm to evaluate broader exposure levels of ALTO-101.

Many of the factors that cause, or lead to, a delay in the commencement or completion of, or the termination or suspension of, clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with 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 currently conduct preclinical testing of our patch formulation drug/device combination product candidate with our collaborator MedRx and may in the future, conduct preclinical and clinical research in collaboration with other academic, pharmaceutical, and biotechnology entities in which we combine our 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.

In addition, certain of our primary or secondary endpoints in our clinical trials, including our currently ongoing Phase 2b clinical trials of ALTO-100 in patients with bipolar depression and ALTO-300, our currently ongoing Phase 2 clinical trial of ALTO-101 in patients with CIAS, and our currently ongoing Phase 2 clinical trial of ALTO-203 in patients with MDD, involve subjective assessments by physicians and/or patients, which can increase the uncertainty of clinical trial outcomes. For example, primary endpoints include the change in MADRS score from baseline to week six, which requires patients or examiners to undertake a questionnaire regarding ten symptoms at the beginning and end of the trial. This and other assessments are inherently subjective, which can increase the variability of clinical results across clinical trials and create a significant degree of uncertainty in determining overall clinical benefit. Such subjectivity may cause the indications we study to be more difficult to evaluate than indications for which clinical trials are structured with more objective endpoints, as such indications are often subject to high placebo effect which may make it more challenging to isolate the beneficial effects of our product candidates. Accordingly, these subjective assessments can complicate clinical trial design, adversely impact the ability of a study to show a statistically significant improvement, and generally adversely impact a clinical development program by introducing additional uncertainties.

Our product development costs will increase if we experience delays in clinical testing or marketing 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.

***We may find it difficult to enroll patients in our clinical trials. If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

Patient enrollment is a significant factor in the timing of clinical trials, and the timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials to such trial's conclusion as required by the FDA or comparable foreign regulatory authorities. Subject enrollment is affected by many factors including the size and nature of the patient population, competing clinical trials in the same or similar indications or at the same trial site, the severity of the disease or condition under investigation, the availability and efficacy of approved drugs and diagnostics for the disease or condition under investigation, the number and location of clinical sites, the proximity of patients to clinical sites, willingness of patients to participate in a decentralized clinical trial, should we conduct future trials in this manner, the eligibility and exclusion criteria for the trial, perceived risks and benefits of the product candidate under study, the design of the clinical trial, continued enrollment of prospective patients by clinical trial sites, the risk that enrolled patients will not complete a clinical trial, our ability to recruit clinical trial investigators with the appropriate competencies and experience, efforts to facilitate timely enrollment in clinical trials, patient referral practices of physicians, the ability to monitor patients adequately during and after treatment, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new products that may be approved for, or any product candidates under investigation for, the indications we are investigating.

We will be required to identify and enroll a sufficient number of subjects for each of our clinical trials. Utilizing our Platform, we plan to focus our development activities on patients characterized by a biomarker that we believe will be most likely to respond to our product candidates. As a result, the potential patient populations for our clinical trials may be narrowed, and we may experience difficulties in identifying and enrolling a sufficient number of patients in our clinical trials. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or comparable foreign regulatory authorities. In addition, the process of finding and diagnosing subjects may prove costly.

We have in the past and may in the future experience participant withdrawals or discontinuations from our trials. Withdrawal of participants from our clinical trials, including participants in any control groups, may compromise the quality of our data. Even if we are able to enroll a sufficient number of participants in our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials, and delays in enrollment 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. Additionally, participants with neuropsychiatric disorders, including MDD, BPD, and schizophrenia, constitute a vulnerable patient population and 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 relating to their underlying disease or condition or otherwise. Further, subjects in MDD trials historically have been documented to show varying levels of medication compliance in such trials. If subjects are not compliant within a trial, the outcome of such trial may not properly reflect the actual effect of the relevant product candidate.

Additionally, other pharmaceutical companies targeting these same diseases are recruiting clinical trial patients from similar patient populations, which may make it more difficult to fully enroll any clinical trials. Our inability to enroll a sufficient number of patients for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, we expect to rely on clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will have limited influence over their actual performance.

We cannot assure you that our assumptions used in determining expected clinical trial timelines are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

***Use of our product candidates could be associated with adverse side effects, adverse events, or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a product candidate, limit the commercial profile of an approved product, or result in other significant negative consequences that could severely harm our business, prospects, operating results, and financial condition.***

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities, or, if such product candidates are approved, result in a more restrictive label and other post-approval requirements. Any treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial, or could result in potential product liability claims. Any of these occurrences may harm our business, financial condition, and prospects significantly.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials, we may need to interrupt, delay, or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective.

Patients in our ongoing and planned clinical trials may in the future suffer significant adverse events or other side effects not observed in our preclinical studies or previous clinical trials. If such significant adverse events or other side effects are observed in any of our ongoing or planned clinical trials, we may have difficulty recruiting patients to the clinical trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, other comparable regulatory authorities, or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Even if the side effects do not preclude the product candidate from obtaining or maintaining regulatory approval, undesirable side effects may inhibit market acceptance due to tolerability concerns as compared to other available therapies. Any of these developments could materially harm our business, financial condition, 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 Risk Evaluation and Mitigation Strategy, or 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 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 adverse events 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 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;
- we may be required to create a medication guide outlining the risks of a product for patients, or to conduct post-marketing studies;
- we may be required to change the way a product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or be sued and held liable for harm caused to subjects or patients; and
- a product may become less competitive, and our reputation may suffer.

In addition, participants with neuropsychiatric disorders, including MDD, BPD, and schizophrenia, constitute a vulnerable patient population and any adverse side effects or adverse events may be exacerbated in such patient population. 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 other regulatory authorities.

***We rely heavily on the biomarker data gathered from our Platform. We currently anticipate that certain of our therapeutic product candidates will require us to develop and obtain FDA approval of a companion diagnostic for such therapeutic product candidates. If the FDA does not agree with our approach, or if we are unable to successfully develop and obtain regulatory approval for certain companion diagnostic tools needed to leverage our Platform, or experience significant delays in doing so, our business will be materially harmed.***

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, along with the companion diagnostic tools needed to leverage our Platform. Our development programs contemplate the use of our Platform, which uses machine learning to identify appropriate patient populations. Our Platform measures biomarkers by analyzing factors such as brain activity patterns detected via EEG readings, cognitive assessment scores, and sleep structure and circadian rhythms captured by wearable data. Analyzing a broad range of biomarkers allows our scientists to develop a comprehensive understanding of the underlying mechanisms of mental health conditions, and target these accordingly. Companion diagnostics, which come in many forms, are the tests needed to identify these biomarkers and, thus, identify an appropriate patient population for our product candidates. The process of obtaining or creating such diagnostic is time consuming and costly. Absent an exemption, these companion diagnostics will be subject to regulation and marketing approval or clearance as medical devices by the FDA and comparable foreign regulatory authorities before we may commercialize our product candidates.

In the United States, the laws and regulations governing the marketing of companion diagnostics are evolving, extremely complex, and in many instances, there are no significant regulatory or judicial interpretations of these laws and regulations. We currently anticipate that certain of our therapeutic product candidates will require us to develop and obtain FDA approval of a companion diagnostic for such therapeutic product candidates. This includes certain software applications, such as software that we are developing to identify biomarkers, that may meet the definition of a medical device and be subject to FDA premarket authorization, depending on its classification and software function. The approval or clearance of the therapeutic with a labeled limitation on use in only those patients who receive certain results using a companion diagnostic will limit the marketing of the product candidate, if approved, to only those patients who express the biomarker detected by the companion diagnostic. We expect to initiate discussions with the FDA concerning the development of companion diagnostics at our end of Phase 2 meetings with respect to ALTO-100 and ALTO-300. See "Item 1. Business—Government Regulation—FDA Regulation of Companion Diagnostics and Clinical Decision Support Software" in this Annual Report.

Moreover, even if data from early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion

diagnostic. We and/or third-party collaborators may encounter difficulties in developing, obtaining regulatory approval or clearance for, manufacturing, and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving marketing authorization, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we or any third parties we may engage are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so:

- we may be unable to identify appropriate patients for enrollment in our clinical trials, which may adversely affect the development of our product candidates;
- our product candidates may not receive marketing approval if the FDA or other regulators determine that the safe and effective use of our product candidates, if any, depends on the companion diagnostic; and
- we may not realize the full commercial potential of any therapeutics that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our medicines, if any.

If we are unable to develop and obtain regulatory approval or clearance for the companion diagnostic tools needed to leverage our Platform, our business, financial condition, results of operations, and prospects could be materially and adversely affected.

***Our approach to the discovery and development of precision medicines based on our Platform is unproven, and we do not know whether we will be able to develop any therapeutics or companion diagnostics of commercial value, or if competing technological approaches will limit the commercial value of our product candidates and Platform.***

We have concentrated our research and development efforts on the application of precision medicine to the diagnosis and treatment of psychiatric disorders, including MDD, BPD, and schizophrenia, and our future success depends on the discovery of biomarkers through our Platform and the continued development of this Platform. However, neither we nor any other company has received regulatory approval to market therapeutics targeting specific subpopulations of patients with psychiatric disorders based on biomarker identification. The success of our business depends primarily upon our ability to identify, develop, and commercialize precision medicine products based on our Platform, which leverages a novel and unproven approach of applying data analytics and machine learning to the thousands of samples available to us through data collected from both our trials and third party trials. We have not yet succeeded and may not succeed in demonstrating efficacy for any product candidates in clinical trials (e.g., we reported negative topline results in October 2024 with regard to our Phase 2b trial of ALTO-100 in MDD) or in obtaining marketing approval thereafter. Our research methodology and novel approach to precision medicine for MDD, BPD, and schizophrenia may be unsuccessful in identifying biomarkers that lead to effective selection of a specific subpopulation of patients for whom a product candidate would be effective. Further, even if we successfully identify biomarkers that can be used to identify a specific subpopulation of patients for whom a product candidate would be effective, we may not be able to test potential patients for biomarkers on a commercial scale. Additionally, the FDA may not agree with our biomarker-based approach, which would present additional risks to the potential for successful development. Moreover, because all of our product candidates and development programs utilize our Platform, adverse developments with respect to one of our programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other programs.

In addition, the biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies. Our future success will depend in part on our ability to maintain a competitive position for our Platform, which relies on our ability to establish predictive biomarkers and segment patients into biomarker-characterized populations corresponding to product candidates in our pipeline. If our Platform is compromised, it may materially and adversely affect our ability to create and develop product candidates and identify biomarkers, and compete effectively. Our competitors may render our approach obsolete, or limit the commercial value of our product candidates and identified biomarkers, by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

***We have never commercialized a product candidate and may experience delays or unexpected difficulties in obtaining, or fail to obtain, regulatory approval for our product candidates.***

We have never obtained regulatory approval for, or commercialized, a drug. Our clinical trial results may not support regulatory 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 or the use of biomarkers to identify patient populations who will benefit from our product candidates;
- 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;
- negative or ambiguous results from our clinical trials, or results may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials that are conducted at clinical facilities or in countries where the standard of care is potentially different from that of their own country;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the 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, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- 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;
- additional time may be required to obtain marketing authorization for any of our product candidates that are regulated as a drug/device combination product;
- such authorities may not accept a submission due to, among other reasons, the content or formatting of the submission; and
- the FDA or comparable foreign regulatory authorities may find deficiencies in or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies.

In addition, the product candidate we are developing as ALTO-300 is already an approved antidepressant in Europe and Australia with the International Nonproprietary Name agomelatine. While we are developing ALTO-300 solely in the United States, if there is a recall, safety concern, or adverse regulatory action with respect to agomelatine in Europe or Australia, it could adversely affect our ability to obtain regulatory approval for ALTO-300 in the United States.

Finally, the FDA and comparable foreign regulatory authorities may change their approval policies and new regulations may be enacted, which could delay or prevent our ability to obtain approval. If any of our product candidates fail to achieve regulatory approval due to the above factors, or otherwise, any such failure would adversely affect our business, results of operations, and financial condition. In addition, difficulties in obtaining approval of a product candidate in any of the initial indications for which we are developing it could adversely affect our efforts to seek approval from regulatory authorities for other indications.

***Additional time may be required to obtain marketing authorizations for any of our product candidates that we develop as drug/device combination products.***

We are developing one of our product candidates, ALTO-101, as a drug/device combination product candidate. While we have not had conversations to date with the FDA regarding whether ALTO-101 would be regulated as a combination product, we anticipate that, if successfully developed, ALTO-101 would be regulated as a combination product by the FDA and other regulatory authorities. Combination products require coordination within the FDA and within comparable regulatory agencies for review of their drug and device components. For example, the FDA's review of a marketing application for ALTO-101 may include the participation of both the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health. Although the FDA and comparable foreign agencies have or may have systems in place for the review and approval of combination products, we may experience additional delays in the development and commercialization of such product candidates due to regulatory timing constraints and uncertainties in the product development and approval process. Moreover, although we anticipate that the device component of any combination product candidates we develop will be reviewed within the usual time frames expected for the underlying drug component application, and that no separate marketing application for the device components of such product candidates will be required in the United States, the FDA or comparable regulatory authorities may delay approval or require us to conduct additional studies with the device which may delay the approval of the combination product.

***Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us or any future collaboration partners from obtaining approvals for the commercialization of our product candidates.***

Any product candidate we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, import, export, marketing, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable foreign regulatory authorities. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of the product candidates we may seek to develop in the future will ever obtain regulatory approval. We have no experience in filing and supporting the applications necessary to gain marketing approvals. Although we believe that we have the capabilities to conduct preclinical studies and clinical trials and complete these applications using our internal resources, we selectively employ and may in the future rely on third-party contract research organizations, or CROs, or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, often takes many years following the commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved, as well as the target indications and patient populations. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Prior to obtaining approval to commercialize a product candidate in the U.S. or abroad, we must demonstrate with substantial evidence from 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. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may delay, limit, or deny approval of a product candidate for many reasons, or may decide that our data are insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Despite the time and expense invested in clinical development of product candidates, regulatory approval of a product candidate is never guaranteed. Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods, and agreements with pricing authorities.

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 REMS, which may be required because the FDA believes it is necessary to ensure safe use of the product after approval.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates, including for other indications, may be harmed, and our ability to generate revenues will be materially impaired.

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

From time to time, we may publicly disclose preliminary or topline 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 topline 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. Topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the topline or preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. For example, in February 2025, we reported the results of an interim analysis of our clinical trial of ALTO-300 in MDD. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as participant 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 and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and could 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, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, financial condition, results of operations, and prospects. Further, disclosure of interim, topline, or preliminary data by us or by our competitors could result in volatility in the price of our common stock.

Furthermore, if we fail to replicate the positive results from our preclinical studies or clinical trials in our future clinical trials, we may be unable to successfully develop, obtain regulatory approval for, and commercialize our current or future product candidates.

***If we fail to develop and commercialize our current product candidates for additional indications or fail to discover, develop, and commercialize other product candidates, we may be unable to grow our business and our ability to achieve our strategic objectives would be impaired.***

Although the development and commercialization of our current product candidates for the treatment of MDD, BPD, and schizophrenia are our primary focus, as part of our longer-term growth strategy, we plan to potentially evaluate our current product candidates in other indications and develop other product candidates. We intend to evaluate internal opportunities from our current product candidates or other potential product candidates, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from other disorders with significant unmet medical needs and limited treatment options. These other potential product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials, and approval by the

FDA and/or comparable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products, if approved, will be manufactured or produced economically, successfully commercialized, or widely accepted in the marketplace, or be more effective than other commercially available alternatives.

Research programs to identify product candidates require substantial technical, financial, and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

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

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth and achieving our strategic objectives may be impaired.

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

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

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

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

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

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive and maintain applicable marketing approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed, which could adversely affect our business, results of operations, and financial condition.

***We may conduct certain of our clinical trials for our product candidates outside of the United States. However, the FDA may not accept data from such trials, in which case our development plans may be delayed, which could materially harm our business.***

We may conduct one or more of our clinical trials for our product candidates outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, to accept data from a clinical trial that was conducted only at sites outside of the United States and not subject to an IND, the FDA requires such clinical trial to have been conducted in accordance with GCPs, and the FDA must be able to validate the data from the clinical trial through an on-site inspection if the FDA deems such inspection necessary. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. For studies not subject to an IND, the FDA generally does not review clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design, protocol, and/or results from a non-U.S. clinical trial were inadequate for the purposes we intend, which could require us to conduct additional clinical trials. Many foreign regulatory authorities have similar requirements for clinical data gathered outside of their respective jurisdictions. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance the FDA or any comparable foreign regulatory authority will accept data from clinical trials conducted outside of the United States or the relevant jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept data from our clinical trials of our product candidates, it may result in the need for additional clinical trials, which would be costly and time consuming and delay or permanently halt our development of our therapeutic product candidates.

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

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment, and storage requirements;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

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

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, testing for biomarkers and pairing biomarker identification with our product candidates may not gain acceptance among physicians, patients, third-party payors, and others in the medical community. If both our approach to precision psychiatry and product candidates for which we obtain regulatory approval do not gain an adequate level of market acceptance, we may not generate sufficient product revenue or become profitable. Further, the number of patients with the relevant biomarkers that our product candidates are designed to treat may be smaller than expected.

The degree of market acceptance of both our approach to precision psychiatry and our product candidates will depend on a number of factors, some of which are beyond our control, including:

- the pricing and cost-effectiveness of our product candidates, as well as the ease of administration, time burden, and market acceptance of testing for biomarkers in relation to alternative treatments and therapies;
- the safety, efficacy, and tolerability of our product candidates;
- acceptance of our approach to precision psychiatry by patients, the medical community, and third-party payors;
- changes in the standard of care for targeted indications and 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 and the ability to test for identified biomarkers;
- the clinical indications for which the products are approved and the approved claims that we may make for the products;
- any restrictions on the use of our products, and the prevalence and severity of any adverse effects;
- distribution and use restrictions imposed by the FDA with respect to such product candidates or to which we agree as part of a mandatory REMS or voluntary risk management plan;
- the availability of adequate coverage and reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- the extent and strength of our marketing and distribution of such product candidates;
- the timing of market introduction of such product candidates, as well as competitive products;
- our ability to offer our product candidates for sale at competitive prices;
- adverse publicity about our product or favorable publicity about competitive products; and
- potential product liability claims.

In addition, the product candidate we are developing as ALTO-300 is already an approved antidepressant in Europe and Australia with the International Nonproprietary Name agomelatine. While we are developing ALTO-300 solely in the United States, if there is a recall, safety concern, or adverse regulatory action with respect to agomelatine in Europe or Australia, it could prevent us from achieving or maintaining market acceptance of ALTO-300 or otherwise adversely affect our ability to successfully commercialize ALTO-300 in the United States.

Our efforts to educate the medical community and third-party payors as to the benefits of both our approach to precision psychiatry and our product candidates may require significant resources and may never be successful. Even if the medical community accepts the ability to test for identified biomarkers and that our products, if approved, 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 for 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.

***The successful commercialization of our product candidates, if approved, will depend in part on the extent to which governmental authorities and health 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, 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 an equivalent generic drug or a less expensive therapy is available. It is possible that third-party payors may not see the benefit of using biomarkers to identify patient populations who will benefit from our product candidates. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products, if approved, and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. Regulatory approvals, pricing, and reimbursement for new drug products vary widely from country to country. 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 drug 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.

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 at short notice, and we believe that changes in these rules and regulations are likely. Thus, even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Some or all of our companion diagnostic tests may require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical products. If any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for our product candidates, if approved.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products. In many countries, the prices of medicinal products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates, if approved. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. See "—Drug marketing and reimbursement regulations in the EU may materially affect our ability to market and receive coverage for our products in the EU member states" below for further discussion of risks related to foreign marketing and reimbursement regulations.

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 any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

## Risks Related to Our Business and Operations

***We were founded with a mission to redefine neuropsychiatric drug development, a field that has seen very limited success. The ability to successfully develop drugs in this field is extremely difficult and is subject to a number of unique challenges.***

Drug development in the field of neuropsychiatry and CNS disorders has seen very limited success historically, with a 7.3% and 6.2% likelihood of approval from Phase 1 in psychiatry and neurology, respectively. Clinical success depends on a number of factors and employing a patient selection biomarker approach does not guarantee that our product candidates will be approved and commercialized. Developing a product candidate for treatment of CNS disorders is extremely difficult and subjects us to a number of unique challenges. For example, clinical trials focused on neuropsychiatric diseases rely on subjective patient-reported outcomes as key endpoints. This makes them more difficult to evaluate than indications with more objective endpoints. Furthermore, these indications are often subject to a placebo effect, which may make it more challenging to isolate the beneficial effects of our product candidates. There can be no guarantee that we will successfully overcome these challenges in our ongoing or any future clinical trials of our product candidates or that we will not encounter other challenges in the development of our product candidates.

Moreover, obtaining regulatory approval from the FDA and other regulatory authorities who only have a limited set of precedents to rely on augments challenges in neuropsychiatric drug development. We intend to work closely with the FDA and comparable foreign regulatory authorities to perform the requisite scientific analyses and evaluation in an effort to obtain regulatory approval for our product candidates; however, the process of developing our product candidates may be more complex and time-consuming relative to other more well-known approaches to drug development. We cannot be certain that our approach will lead to the development of product candidates that effectively and safely address CNS disorders.

Moreover, given the history of clinical failures in this field, future clinical or regulatory failures by us or others may result in further negative perception of the likelihood of success in this field, which may significantly and adversely affect the market price of our common stock.

***Our business depends on the success of our product candidates. If we are ultimately unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.***

We currently have no products approved for commercial sale or for which regulatory approval to market has been sought. We have invested a significant portion of our efforts and financial resources in the development of our product candidates, each of which is still in clinical development, and expect that we will continue to invest heavily in these product candidates, as well as in any future product candidates we may develop. Our business 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.

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

- scale our ability to test potential patients for biomarkers so that we can identify patients for whom we believe our product candidates would be effective;
- demonstrate the superiority of pairing biomarker identification with our product candidates compared to the standard of care, as well as other therapies in development;
- achieve market acceptance of our Platform by patients, the medical community, and third-party payors;
- create market demand for our product candidates through our 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;
- price our products competitively such that third-party and government reimbursement permits broad product adoption;
- effectively commercialize any of our products that may receive regulatory approval;

- manufacture or otherwise have access to EEG testing mechanisms that can be used by physicians and patients to test for identified biomarkers;
- 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;
- maintain compliance with applicable laws, regulations, and guidance specific to commercialization including interactions with health care professionals, patient advocacy groups, and communication of health care economic information to payors and formularies; and
- assure that our products, if approved, will be used as directed and that additional unexpected safety risks will not arise.

***We rely on, and intend to continue to rely on, our internal clinical development expertise to conduct our current and future clinical trials. This model includes internal teams and systems as well as external vendors and CROs to comprise a full clinical trial team. If our clinical trial team does not comply with applicable regulatory requirements, meet expected deadlines, or run trials effectively, our development programs and our ability to seek or obtain regulatory approval for or commercialize our product candidates may be delayed.***

We conduct much of our clinical trial work (*e.g.*, clinical and medical monitoring, data management, and project management) with internal personnel, though we selectively employ CROs when conducting our Phase 1 pharmacodynamic trials and use certain CRO and/or vendor services (*e.g.*, biostatistics, pharmacovigilance, central raters, and rater training and remediation services) to augment our internal expertise. We also rely on our internal, proprietary systems for some data, Spectra, Altoscope, and TechCheck. See "Item 1. Business—Our Platform." Moreover, some of our trials have included in the past, and may include in the future, a decentralized clinical trial component supported by our internal personnel wherein clinical trial activity occurs in the participant's home or at a local health care facility and includes virtual elements of care, exposing us to increased risk of variability and lack of control of the clinical trial.

Although we believe that we have the capabilities to conduct clinical trials through our insourced model, we may need to rely on third party CROs to conduct clinical trials if our internal capabilities cannot scale as we work to progress our current product candidates through development, as we potentially expand our product candidate portfolio, or if we do not have sufficient or applicable personnel to support any future potential decentralized clinical trials. Moreover, without the use of an experienced CRO, our insourced team is responsible for the coordination of drug supply through various shipping vendors, the supply of certain equipment (*e.g.*, EEG devices) for our trials, and the management of potential future decentralized clinical trials; our failure to coordinate such matters in an effective and efficient manner could have a material adverse effect on our trials, including our ability to execute upon any future potential decentralized clinical trials. Our failure or the failure of any CROs we may employ to conduct the trials in compliance with FDA regulations could result in a delay or failure in obtaining FDA approval and could require us to repeat any preclinical studies or clinical trials we or the CRO administered. Our insourced personnel could fail to meet deadlines or run less effectively than a CRO, which could delay development of our product candidates and our ability to seek or obtain regulatory approval or marketing approval for our product candidates.

Further, under our insourced model we presently contract directly with all of our clinical trial sites, and therefore have to negotiate budgets and contracts with each trial site, which may result in delays to our development timelines and increased costs. If any of our relationships with trial sites terminate, we may not be able to enter into arrangements with alternative trial sites or do so on commercially reasonable terms. Switching or adding additional trial sites can also involve additional costs and requires time and focus of our clinical trial operations management team.

Additionally, if we ever transition to relying on a CRO to manage the conduct of any of our clinical trials, we will also have to negotiate budgets and contracts with such CRO, which may similarly lead to delays and increased costs. There is a natural transition period when a new CRO begins work which could result in delays that could materially impact our ability to meet our desired clinical development timelines.

***The terms of our Amended Loan Agreement and our Convertible Grant Agreement place restrictions on our operating and financial flexibility and may cause dilution to our stockholders. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business or result in further dilution to you.***

In December 2022, we entered into a loan and security agreement, or the Original Loan Agreement, with K2 HealthVentures, as a lender and the other lenders from time to time party thereto, or collectively, the Lender, K2 HealthVentures, as administrative agent for the Lender, and Ankura Trust Company, LLC, as collateral agent for the Lender. In January 2025, we entered into an amendment to this facility, or the Amendment (and collectively with the Original Loan Agreement, the Amended Loan Agreement), pursuant to which the Lender has agreed to make available to us term loans in an aggregate principal amount of up to $75.0 million, including a $20.0 million tranche funded on January 13, 2025 (approximately $10.0 million of which was used to refinance all obligations under the Original Loan Agreement and pay fees and expenses incurred in connection with the Amendment). Based upon the terms of the Amended Loan Agreement, up to an additional $30.0 million is available at our request until December 15, 2025, subject to our achievement of certain milestones as more fully described in the Amended Loan Agreement, and up to an additional $25.0 million is available at our request subject to the Lender's approval. Our obligations under the Amended Loan Agreement are secured by a security interest in substantially all of our assets, other than intellectual property assets. The Amended Loan Agreement includes customary affirmative and negative covenants, as well as standard events of default, including an event of default based on the occurrence of a material adverse event. The negative covenants include, among others, restrictions on our ability to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay cash dividends or make other distributions, make investments, create liens, sell assets, and make any payment on subordinated debt, in each case subject to certain exceptions. In addition, following an initial period with no financial covenants, beginning January 1, 2026, we must maintain a cash runway of at least five months, provided that this covenant will be waived during any period in which our market capitalization exceeds $700.0 million. These restrictive covenants could limit our flexibility in operating our business and our ability to pursue business opportunities that we or our stockholders may consider beneficial and failure to comply with these restrictive covenants would make us ineligible to receive future additional funding under the Amended Loan Agreement.

In July 2024, we entered into a convertible loan agreement, or the Convertible Grant Agreement, with The Wellcome Trust Limited, or Wellcome. The Convertible Grant Agreement provides for an unsecured convertible loan, or the Convertible Loan, from Wellcome of up to approximately $11.7 million, payable in six tranches, $1.3 million of which was funded upon the execution of the Convertible Grant Agreement, and the remainder of which will be funded upon draw down of the remaining initiation payment or the completion of certain milestones as set forth in the Convertible Grant Agreement, subject to certain conditions described therein which may or may not be met in a timely manner or at all. Proceeds from the Convertible Loan may be used by the Company solely to advance development of ALTO-100 in bipolar depression. The Convertible Grant Agreement also includes customary covenants, representations and warranties, including with respect to the conduct of our Phase 2b clinical trial evaluating ALTO-100 in patients with bipolar depression and certain information and audit rights of Wellcome in connection therewith, as well as with respect to our efforts to develop and exploit ALTO-100.

The Lender could declare a default upon the occurrence of any event that it interprets could have a material adverse effect, as defined in the Amended Loan Agreement, and Wellcome may declare an event of default upon the occurrence of certain specified events set forth in the Convertible Grant Agreement. Upon the occurrence and continuance of an event of default, the Lender or Wellcome, as applicable, may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Amended Loan Agreement and the Convertible Grant Agreement, respectively. Any declaration of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay these outstanding obligations at the time any event of default occurs. Further, if we raise any additional capital through debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

In addition, pursuant to the Amended Loan Agreement, the Lender may, at its option, elect to convert up to $9.0 million of the then outstanding term loan amount into shares of our common stock. The Lender also has warrants to purchase shares of our common stock, and we may be required to issue additional warrants to the Lender in the future. At any time after the second anniversary of the date of the Convertible Grant Agreement, Wellcome has the right, from time to time, to convert some or all of the Convertible Loan into shares of our common stock at a 20% discount to the 30-day volume-weighted average price on the New York Stock Exchange at the date of conversion. Any conversion of debt into equity by the Lender

or Wellcome pursuant to the Amended Loan Agreement or the Convertible Grant Agreement, respectively, or exercise of any warrants held by the Lender now or in the future would cause dilution to our stockholders.

***Competitive products may reduce or eliminate the commercial opportunity for our product candidates for our current or future indications. If our competitors develop technologies or product candidates more rapidly than we do, or their technologies are more effective or safer than ours, our ability to develop and successfully commercialize our current products may be adversely affected.***

The biopharmaceutical industry is characterized by the rapid innovation and intense competition. While we believe that our innovative precision psychiatry approach and pipeline of clinical assets provide us with competitive advantages, we face competition from multiple biopharmaceutical and biotechnology companies that are similarly working to develop therapeutics targeting neuropsychiatry and CNS disorders, as well as from academic institutions, governmental agencies, and public and private research institutions. Many of our potential competitors, either alone or with collaboration partners, have significantly greater financial 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 we are in achieving regulatory approvals and commercializing their products. 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. In particular we are developing our product candidates in the areas of major depressive disorder, bipolar depression, and schizophrenia. Notable examples of companies with either approved therapies or product candidates in development in areas that may be competitive in our areas of focus are AbbVie Inc.; Axsome Therapeutics, Inc.; Neumora Therapeutics, Inc.; Neurocrine Biosciences, Inc.; and Xenon Pharmaceuticals, Inc., among others.

We believe the key competitive factors affecting the success of our product candidates that we develop to address MDD, BPD, schizophrenia, and other CNS disorders, if approved, are likely to be efficacy, safety, convenience, price, the level of generic competition, and the availability of reimbursement from government and other third-party payors. Our profitability and financial position will suffer if our product candidates receive regulatory approval but cannot compete effectively in the marketplace.

***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 76 total employees. As our development and commercialization plans and strategies develop, and as we transition into fully operating as a public company, we expect to expand our employee base for managerial, operational, financial, and other resources. In addition, we have limited experience in manufacturing and commercialization. As our product candidates enter and advance through clinical trials, we will need 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 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, which may lead to significant costs and may divert management attention. 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 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 our Founder, President, and Chief Executive Officer, Amit Etkin, M.D., Ph.D., and other members of our 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 maintain “key person” life insurance for

Dr. Etkin, but the insurance proceeds may not be sufficient to compensate for the adverse effects that we expect would arise from the loss of Dr. Etkin and the costs associated with recruiting a new Chief Executive Officer.

Additionally, in light of our insourced clinical trial model, we are heavily reliant on the expertise of our clinical trial team, and the loss of even a small number of those employees could have a significant adverse impact on our ability to conduct our clinical trials in a compliant and timely manner. Additionally, as we expand our clinical trial operations, or if we experience turnover within our clinical trial team, even if we are able to recruit qualified personnel to support our insourced clinical trial model, the onboarding and integration process takes time and can result in delays to our clinical development timeline.

We will need 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 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 current and any future employees, independent contractors, consultants, commercial partners, CROs, CMOs, and vendors. 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, European Medicines Agency, and other comparable foreign regulatory authorities, 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 of any of 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. 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, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, 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, United Kingdom and Japan, for which we may rely on collaboration with third parties. We are not permitted to market or promote any of 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 any of 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 marketing approvals, our target market will be reduced and 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 of any of 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 the 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 obtaining approval for, and market, our products, such claims could result in an investigation by the FDA, comparable foreign regulatory authorities, or other regulators of the safety and efficacy 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 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 any 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 any 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.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include property, general liability, clinical trials, cybersecurity, 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 may seek Breakthrough Therapy Designation by the FDA for a product candidate that we develop, and we may be unsuccessful. If we are successful, the designation may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.***

We may seek Breakthrough Therapy Designation for our product candidates where we believe the clinical data support such designation. A "Breakthrough Therapy" designation may be available for a drug candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, increased interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as Breakthrough Therapies by the FDA also receive the same benefits associated with Fast Track Designation, including eligibility for rolling review of a submitted NDA, if the relevant criteria are met.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of the product candidates we develop qualify as Breakthrough Therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification and rescind the designation, or otherwise decide that the time period required for FDA review or approval will not be reduced.

***We may seek Fast Track Designation by the FDA for a product candidate that we develop, and we may be unsuccessful. If we are successful, the designation may not actually lead to a faster development or regulatory review or approval process, and would not increase the likelihood that our product candidates will receive marketing approval.***

We may seek Fast Track Designation for the product candidates we develop. The Fast Track program is intended to expedite or facilitate the process for reviewing new product candidates that meet certain criteria. Specifically, if a new drug is intended for the treatment of a serious or life-threatening disease or condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition, the drug sponsor may apply for Fast Track Designation.

Fast Track Designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. An NDA submitted for a Fast Track product candidate may also be eligible for rolling review, where 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 application. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation for any of our product candidates, such product candidates may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may also withdraw the Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Furthermore, such a designation does not increase the likelihood that any product candidate that may be granted Fast Track Designation will receive regulatory approval in the United States. Many product candidates that have received Fast Track Designation have ultimately failed to obtain approval.

***If our telecommunications or information technology systems, or those used by our collaborators, CROs, CMOs, clinical sites, third-party logistics providers, distributors, or other contractors, consultants, or third party service providers upon which we rely, are or were compromised, become unavailable, or suffer security breaches, loss, or leakage of data or other disruptions, we could suffer adverse consequences resulting from such compromise, including but not limited to, operational or service interruption, harm to our reputation, litigation, fines, penalties and liability, compromise of sensitive information related our business, and other adverse consequences.***

In the ordinary course of our business, we, and the third parties with whom we work, collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, "process") sensitive data and as a result, we and the third parties with whom we work face a variety of evolving threats that could cause security incidents and other disruptions to such information technology systems. If any of our sensitive or proprietary data is compromised, including our Platform and our internal, proprietary systems for data collection, it may materially and adversely affect our ability to create and develop product candidates and identify biomarkers, and compete effectively.

Our Platform, our internal, proprietary systems for data collection, and our information technology systems and those of our collaborators, CROs, CMOs, clinical sites, third-party logistics providers, distributors, and other contractors and consultants upon which we rely are vulnerable to attack, damage, and interruption from cyberattacks, computer viruses, bugs, worms, or other malicious codes, malware (including ransomware, and as a result of advanced persistent threat intrusions), model poisoning, and other attacks by computer hackers, nation-state and nation-state-supported actors, cracking, application security attacks, social engineering (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), supply chain attacks and vulnerabilities through our third-party service providers, denial- or degradation-of-service attacks, credential stuffing attacks, credential harvesting, personnel misconduct or error, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications or electrical failures, natural disasters (*e.g.*, earthquakes, fires, and floods), terrorism, war, attacks enhanced or facilitated by artificial intelligence, and other similar threats. Such systems are also vulnerable to intentional or inadvertent acts or lack of action by those with authorized access to our systems that could lead to exposure or exploitation of those systems.

Such threats are prevalent and continue to rise, 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, and the diversion of funds. 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 cyber-attacks for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, the third parties upon which we rely, and our customers may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell, and distribute our goods and services. In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

Our sensitive information could be leaked, disclosed, or revealed as a result of or in connection with the use by our personnel or vendors of generative artificial intelligence, or AI, technologies. Additionally, remote work has increased risks to our information technology systems and data, as our employees 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 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 companies into our information technology environment and security program.

We and certain of our service providers are from time to time subject to system failures, cyberattacks, and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, and take steps to detect and remediate vulnerabilities, we may not be able to detect, adequately investigate, or remediate all vulnerabilities or breaches because the tools and techniques used to exploit such vulnerabilities change frequently are often sophisticated in nature, and are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred or for an extended period. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

We rely on third-party service providers and technologies to process sensitive information in a variety of contexts, including, without limitation, cloud-based infrastructure, encryption and authentication technology, employee email, and other functions. We also rely on third-party service providers to assist with our clinical trials, provide other products or services, or otherwise to operate our business. 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. If our third-party service providers experience a security incident or other interruption, as some in the past have, we could experience adverse consequences. 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 (including our services) or the third-party information technology systems that support us and our services.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive data or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our services including clinical trials. For example, we have been the target of unsuccessful phishing attempts in the past, and expect such attempts will continue in the future.

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 collaborators, CROs, CMOs, clinical sites, third-party logistics providers, distributors, and other contractors and consultants 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.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from financial, legal, business, or reputational losses or to mitigate other liabilities arising out of an interruption or breach of our systems, or deficiencies in our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

If any such incidents were to occur and cause interruptions in our operations, it could result in a material 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 unauthorized disclosure of personal, confidential, or proprietary information, we could incur liability, including litigation exposure, penalties, and fines, we could become the subject of regulatory action or investigation, our competitive position could be harmed and the further development and commercialization of any product candidates could be delayed. Such incidents could also expose us to risks, including an inability to provide our services and fulfill contractual demands, and could cause management distraction and the obligation to devote significant financial and other resources to mitigate such problems, which would increase our future information security costs, including through organizational changes, deploying additional personnel, reinforcing administrative, physical, and technical safeguards, further training of employees, changing third-party vendor control practices, and engaging third-party subject matter experts and consultants and reduce the demand for our technology and services. Applicable data privacy and security obligations may require us to notify relevant stakeholders, including affected individuals, customers, regulators, and investors, of security incidents, or to take other actions, such as providing credit monitoring and identity theft protection services. The costs associated with the investigation, remediation, and potential related obligations could be material, and the failure to comply with such requirements could lead to adverse consequences. Any such event could also result in legal claims or proceedings, liability under laws that protect the privacy of personal information, regulatory investigations, and enforcement actions, including significant regulatory penalties, 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 materially and adversely affect our business, results of operations, or financial condition.

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

Our current corporate and IT infrastructure operations are predominantly located in California. Any unplanned event, such as flood, wildfire, explosion, earthquake, extreme weather condition, medical epidemic, power shortage, telecommunication failure, or other natural or man-made 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 man-made disasters on our current or future third-party 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 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 we and our current or future CMOs and CROs 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 label for each of our product candidates approved for sale for these indications, if any, the ability to scale testing for identified biomarkers, 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 through biomarker identification, and 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.

***Our business could be adversely affected by the effects of health pandemics or epidemics, which could cause significant disruptions in our operations and those of our current or future CMOs, CROs, and other third parties upon whom we rely.***

Health pandemics or epidemics have in the past and could again in the future result in quarantines, stay-at-home orders, remote work policies, or other similar events that may disrupt businesses, delay our research and development programs and timelines, negatively impact productivity and increase risks associated with cybersecurity, the future magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations. More specifically, these types of events may negatively impact personnel at third-party manufacturing facilities or the availability or cost of materials, which could disrupt our supply chain. Moreover, our trials may be negatively affected. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources. Some patients may not be able or willing to comply with trial protocols if quarantines impede patient movement or interrupt healthcare services. Our ability to recruit and retain patients, principal investigators, and site staff (who as healthcare providers may have heightened exposure) may be hindered, which would adversely affect our trial operations. Disruptions or restrictions on our ability to travel to monitor data from our trials, or to conduct trials, or the ability of patients enrolled in our trials or staff at trial sites to travel, as well as temporary closures of our trial partners and CMOs' facilities, would negatively impact our trial activities. In addition, we rely on independent clinical investigators, CROs, and other third-party service providers to assist us in managing, monitoring, and otherwise carrying out certain of our preclinical studies and clinical trials, including the collection of data from our trials, and the effects of health pandemics or epidemics may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us. Similarly, our trials could be delayed and/or disrupted. As a result, the expected timeline for data readouts, including incompleteness in data collection and analysis and other related activities, and certain regulatory filings may be negatively impacted, which would adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and adversely affect our business, financial condition, results of operations, and prospects. In addition, impact on the operations of the FDA or comparable foreign regulatory authorities could negatively affect our planned trials and approval processes. Finally, economic conditions and business activity may be negatively impacted and may not recover as quickly as anticipated.

**Risks Related to Collaborations, Intellectual Property, and Related Agreements**

***If we are unable to obtain and maintain sufficient intellectual property protection for our Platform, technologies, and 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, trade secrets, and confidentiality agreements, to protect the intellectual property related to our Platform, technologies, and product candidates and to prevent third parties from copying and

surpassing our achievements, thus eroding our competitive position in our market. We also rely on protection afforded by in-licensed intellectual property rights and proprietary technology of third parties.

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 novel discoveries and technologies that are important to our business. Although we own and in-license issued patents, our pending and future patent applications, and those licensed to us by third party licensors, may not result in patents being issued. Even if our patent applications result in issued patents, we cannot assure you that such 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 that they will effectively prevent others from commercializing competitive technologies, 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. We do not have exclusive control over the preparation, filing, and prosecution of patent applications under certain of our in-license agreements, and although we may have the right to have some input in connection with such activities, we may not have the right to control the preparation, filing, and prosecution of patent applications that are licensed to us by third parties, or to control prosecution and maintenance of patents that we out-license to third parties. Therefore, patents and applications that are relevant to our product candidates may not be prosecuted and enforced in a manner consistent with the best interests of our business. Although we 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 technologies or 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 any of our or our collaborators' or licensors' 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 or our licensors' issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Further, our issued composition of matter patents covering our pharmaceutical product candidates may expire at such a date that our patents may not prevent competitors from developing, making and marketing a product that is identical to our product candidates after expiration of any applicable regulatory exclusivities. For example, our composition of matter patents in ALTO-100 expired and patents covering its method of manufacturing are due to expire in 2030; our composition of matter patents in ALTO-202 (compound) expired in May 2024 (in foreign countries) and are due to expire in 2026 (in the United States), and our polymorph composition of matter patents in ALTO-202 are due to expire in 2035; and our composition of matter patents in ALTO-203 are due to expire in 2027, in all cases without taking into account patent term extensions or adjustments, and assuming payment of all applicable maintenance, renewal, and annuity fees. Similarly, patents for pharmaceutical formulations containing pharmaceutical product candidates may provide an additional form of intellectual property protection, as such patents provide protection without regard to any method of use. However, we cannot be certain that the claims in our or our collaborators' or licensors' pending patent applications directed to pharmaceutical formulations containing 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 or our licensors' issued patents will be considered valid and enforceable by courts in the United States or foreign countries. In addition, we cannot be certain that the claims of such patents, if granted, will be sufficiently broad to effectively prevent competitors from working around our claimed inventions by developing an alternative formulation and thereby competing with us without infringing our patent rights. Method of use patents protect the use of a product for the specified method or indication. In the absence of separate composition of matter protection, 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 methods of use included in our patents. Moreover, even if competitor products are not approved for use in our patented indications, and our competitors do not actively promote their product for indications that are covered by our patents, clinicians may prescribe these competitor

products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, such infringement is difficult to prevent or prosecute. Like method of use patents, patents relating to our Platform protect the platform for the method specified in the patent claims. This type of patent does not prevent a competitor from developing alternative technologies to identify biomarkers or target patient populations. Even if competitors copy our Platform, infringement may be difficult to determine, 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 and in-licensed patent applications may not result in patents being issued that protect our technologies or product candidates, effectively prevent others from commercializing our technologies or 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 patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we will be successful in protecting our product candidates by obtaining and defending patents. For example, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates or their intended uses, and as a result the impact of such third-party intellectual property rights upon the patentability of our own or our licensors' patents and patent applications, as well as the impact of such third-party intellectual property upon our freedom to operate, is highly uncertain. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or rendered unenforceable. As a result, the issuance, inventorship, scope, validity, enforceability, and commercial value of our or our licensors' patent rights are highly uncertain.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our or our licensors' 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 or our licensors' pending patent applications may be subject to third-party pre-issuance submissions of prior art to the USPTO, and our issued patents and those of our licensors may be subject to post-grant review, proceedings, oppositions, derivations, reexaminations, interferences, *inter partes* review proceedings, or other similar proceedings, in the United States or elsewhere, challenging our or our licensors' 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 or licensed 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 technology and product candidates, or limit the duration of the patent protection of our technology and 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 owned or licensed patent rights are invalid or unenforceable in a litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. An adverse result in any legal proceeding could put one or more of our owned or in-licensed 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 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.

***Issued patents covering our product candidates, or the method of use of our product candidates or associated companion diagnostics could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.***

If we or one of our licensors initiate legal proceedings against a third party to enforce a patent covering our product candidates or companion diagnostics associated with our product candidates, or our other proprietary technologies, including our platform technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity 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, or non-enablement. 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. In addition to such counterclaims, third parties may raise claims challenging the validity or enforceability of a patent before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, derivation proceedings, and equivalent proceedings in foreign jurisdictions (*e.g.*, opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patent rights in such a way that they no longer cover our product candidates, therapeutic and diagnostic programs, and other proprietary or platform technologies we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection provided to our product candidates, companion diagnostics, proprietary platform technologies, or other components of our therapeutic and diagnostic programs, as applicable. Such a loss of patent protection could have a material adverse impact on our business, financial condition, results of operations, and prospects.

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

The growth of our business may depend in part on our ability to acquire, in-license, or use third-party intellectual property and proprietary rights. A number of our existing product candidates are the subject to in-licenses from third parties. Other pharmaceutical companies and academic institutions may own patents or may have filed, or be planning to file, patent applications potentially relevant to our business. In order to avoid infringing such patent rights, we may find it necessary or prudent to obtain licenses to such patent rights from such third parties. For example, we may be required by the FDA or comparable foreign regulatory authorities to provide a specific companion diagnostic test or tests with our product candidates, any of which could require us to obtain rights to use patents or know how owned or controlled by third parties. In addition, with respect to any patent or other intellectual property rights we may co-own with third parties, we may require licenses to such co-owners' interest to such patent or other intellectual property 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 or important to our business operations. In addition, we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. Were that to happen, we may need to cease use of the compositions or methods covered by those third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe, misappropriate, or otherwise violate those intellectual property rights, which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, which means that our competitors may also receive access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, 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. There can be no assurance that we will be able to successfully complete these types of negotiations and ultimately acquire the rights to the intellectual property related to the products or product candidates that we may seek to develop or market. If we are unable to successfully obtain rights to required third-party

intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of certain programs and our business, financial condition, results of operations, and prospects could suffer.

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. 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, 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.

***Our rights to develop and commercialize our product candidates, our Platform, or other technologies are subject, in large part, to the terms and conditions of licenses granted to us by others, such as Stanford, Sanofi, and MedRx. The terms of these licenses may be inadequate to protect our competitive position on products or product candidates for a sufficient amount of time. Further, if we fail to comply with our obligations in the 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 are heavily reliant upon licenses to certain patent rights and other intellectual property that are relevant to our Platform or are important or necessary to the development of ALTO-101 or our other current or future biomarker platform and product candidates. For example, we depend on licenses from Sanofi and MedRx for certain intellectual property relating to the development and commercialization of ALTO-101. Although we conduct diligence on intellectual property that is the subject of our in-licenses at the time of entry into the applicable agreements, these third party licensors may have relied upon, and any future licensors may rely upon, third-party companies, consultants, or collaborators, or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If our 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 ALTO-101 or our other current or future product candidates that are or may be the subject of such licensed rights could be adversely affected. Further development and commercialization of ALTO-101 and development of any future product candidates may, require us to enter into additional license or collaboration agreements. Additionally, under the terms of the Stanford Agreement, we obtained a worldwide, royalty-bearing license, with the right to sublicense during the exclusive term only, under certain patent rights in five patent families relating to brain stimulation, electroencephalogram and functional MRI that are applicable to guiding treatment of psychiatry patients in our Platform, or the Stanford Licensed Patents, and under certain technology relating to the inventions covered by the Stanford Licensed Patents, or Stanford Licensed Technology, to make, have made, use, import, offer for sale and sell licensed products for use in any indication. Our rights under the Stanford Licensed Patents are only exclusive until December 2029, at which time such rights will become non-exclusive, and our rights under the Stanford Licensed Technology are non-exclusive. Our future licenses may not provide us with exclusive rights to use the licensed patent rights and other intellectual property licensed thereunder, or may not provide us with exclusive rights to use such patent rights and intellectual property in all relevant fields of use and in all territories in which we wish to develop or commercialize our product candidates in the future.

These existing license agreements impose, and any future license agreements we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, or other obligations on us. If we breach any of our obligations under our license agreements, including diligence obligations with respect to development and commercialization of product candidates covered by the intellectual property licensed to us, or use the intellectual property licensed to us in an unauthorized manner or we are subject to bankruptcy-related proceedings, we may be required to pay damages and the licensor may have the right to terminate the respective agreement or materially modify the terms of the license, such as by rendering currently exclusive licenses non-exclusive. License termination or modification may result in our inability to develop, manufacture, and commercialize platforms, product candidates and other technology covered by the licensed intellectual property under such license agreements. If such in-license agreements are terminated or modified, or if the underlying patents fail to provide the intended exclusivity, our competitors would 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.

Further, we or our licensors, if any, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. It is possible that defects of form in the preparation or filing of our in-licensed patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our licensors fail to establish, maintain, or protect such in-licensed patent rights or any other in-licensed intellectual property rights, such rights may be reduced or eliminated. If our licensors are not fully cooperative or disagree with us as to the prosecution, maintenance, or enforcement of any in-licensed patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our in-licensed patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial conditions, results of operations, and prospects.

Furthermore, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications that we license from third parties. In certain circumstances, our licensed patent rights are subject to our reimbursing our licensors for their patent prosecution and maintenance costs. If our licensors and future licensors fail to prosecute, maintain, enforce, and defend patents we may license, or lose rights to such patents or patent applications, our licensed rights may be reduced or eliminated. In such circumstances, our right to develop and commercialize any of our platforms, products, or product candidates that is the subject of such licensed rights could be materially adversely affected. Even where we have the right to control prosecution of in-licensed patents and patent applications under license from third parties, we may still be adversely affected or prejudiced by actions or inactions of our predecessors or licensors and their counsel that took place prior to us assuming control over patent prosecution.

Our technology acquired or licensed currently or in the future from various third parties is or may be subject to retained rights. Our predecessors or licensors do and may retain certain rights under their agreements with us, including the right to use the underlying technology for non-commercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our predecessors or licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property that is subject to our existing licenses and compete with our existing product candidates. 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 platforms, product candidates, or other technology infringe, misappropriate, or violate intellectual property rights of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights to third parties, including the terms and conditions thereof;
- our diligence obligations under the license agreement and what activities satisfy those obligations;
- our right to transfer or assign the license;
- the inventorship or ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, our license agreements are, and future license agreements are likely to be, complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of 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 have licensed prevent or impair our ability to maintain our current 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.

Our current or future licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing, misappropriating, or otherwise violating the licensor's intellectual property rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products if infringement or misappropriation were found, those amounts could be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

If we are limited in our ability to utilize acquired or licensed technologies, or if we lose our rights to critical in-licensed technology, we may be unable to successfully develop, out-license, market, and sell our product candidates, which could prevent or delay new product introductions. Our business strategy depends on the successful development of acquired technologies and licensed technology into commercial product candidates. Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out-license, or market and sell our product candidates.

***We may form or seek collaborations or strategic alliances, enter into additional licensing arrangements or other business transactions in the future, and we may not realize the benefits of such transactions.***

We have entered into licensing arrangements and strategic transactions to acquire and advance new assets or product candidates and may consider similar or other types of business arrangements in the future, including strategic partnerships, in-licensing of product candidates, strategic collaborations, joint ventures, restructurings, divestitures, acquisitions of companies, asset purchases, business combinations, and investments.

Any future transactions that we enter into may not be successful. In particular, the success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include 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.

In addition, any future transactions 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.

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 in the future 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.

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

Patents are of national or regional effect. Filing, prosecuting, and defending patents on all of our research programs and product candidates in all countries throughout the world would be prohibitively expensive, and our and our licensors' intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the United States, even in jurisdictions where we or our licensors do pursue patent protection, or from selling or importing products made using our or our licensors' inventions in and into the United States or other jurisdictions. Competitors may use our or our 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 and our 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 and our 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 and our licensors' patents or marketing of competing products in violation of our proprietary rights.

Various countries outside the United States have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. As a result, a patent owner may have limited remedies in certain circumstances, which could materially diminish the value of such patent. If we or our 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.

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 technologies and product candidates. While we will endeavor to try to protect our technologies and product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time consuming, expensive, and unpredictable.

In addition, geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement, or defense of our issued patents or those of any current or future licensors. As a result, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

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

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

- others may be able to make product candidates that are similar to ours, identify different biomarkers or target patient populations, or use product candidates similar to ours with similar biomarker discovery methodologies, but that are not covered by the pending patent applications that we own or the patents or patent applications that we license;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the pending patent application that we own or have exclusively licensed;
- we or our licensors or future 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 biomarker or patient population discovery methodologies without infringing or otherwise violating our owned or licensed intellectual property rights;
- it is possible that noncompliance with the USPTO and foreign governmental patent agencies' requirements 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 or licensed 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 have exclusively licensed 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 and our licensors' patent applications, including whether the patent applications that we own, presently in-license, or, in the future, in-license will result in issued patents with claims that directed to our product candidates or uses thereof in the United States or in other foreign countries;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidates;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents, 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 U.S. and foreign patents and pending patent applications exist in our market that are owned by third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use, and sell our product candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain 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 technologies, 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 technologies or product candidates or will prevent, limit, or otherwise interfere with our ability to make, use, or sell our technologies and 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 biomarker discovery methodologies, 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, misappropriate, or violate our patents, trademarks, or other intellectual property. To counter infringement, misappropriation, or unauthorized use, we or one of our licensing partners 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 our 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 our 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 our 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 our licensors' patent claims do not cover the invention, or decide that the other party's use of our or our 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 our licensors' patents could limit our ability to assert our or our 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, misappropriation, or violation, 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 share price of our common stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to file and pursue such infringement, misappropriation, or violation 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.

***Intellectual property rights of third parties could adversely affect our ability to commercialize our product candidates or any future product candidates, and we, our licensors or collaborators, or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or misappropriation or violation of our other proprietary rights or seeking to invalidate patents or other proprietary rights. We might be required to litigate or obtain licenses from third parties in order to develop or market our product candidates or any future product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms.***

Our commercial success depends, in part, on our ability to develop, manufacture, market, and sell our product candidates and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and other proprietary rights of third parties. Third parties may allege that we have infringed, misappropriated, or otherwise violated their intellectual property. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could adversely affect our ability to compete in the marketplace.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our product candidates. We cannot be certain that our product candidates will not infringe existing or future patents owned by third parties. Third parties may assert infringement claims against us based on existing or future intellectual property rights, regardless of their merit. We may decide in the future to seek a license to such third-party patents or other intellectual property rights, but we might not be able to do so on reasonable terms. Proving patent invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. As this burden is a high one, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent or find that our technologies or product candidates do not infringe any such claims. If we are found to infringe, misappropriate, or otherwise violate a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing, or commercializing the infringing technology or product candidate. Further, we may be required to redesign the technology or product candidate in a non-infringing manner, which may not be commercially feasible. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing, or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our technologies or product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our product candidates, might assert are infringed by our current or future product candidates, including claims to compositions, formulations, methods of manufacture, or methods of use or treatment that cover our product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates, could be found to be infringed by our product candidates. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit, or otherwise interfere with our ability to make, use, and sell our product candidates. The pharmaceutical and biotechnology industries have produced a considerable number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates or methods of use either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents, and there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Even if we are successful in these proceedings, we may incur substantial costs, and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could adversely affect our business and operations. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

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

***Our product candidates licensed from various third parties may be subject to retained rights.***

Our 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. It is difficult to monitor whether any of our licensors limit their use of the product candidates to these permitted uses, and we could incur substantial expenses to enforce our rights to our licensed product candidates in the event of misuse.

In addition, we may license certain rights under the relevant agreements on a non-exclusive basis or we may license exclusive rights that may become nonexclusive after a period of time. For example, under the terms of the Stanford Agreement, our rights under the Stanford Licensed Patents relating to certain Platform patents are exclusive until December 2029, at which time it will become non-exclusive, and our rights under the Stanford Licensed Technology are non-exclusive.

Further, the U.S. federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or Bayh-Dole Act. For examples, certain patents and patent applications licensed from Stanford may have been made with financial assistance from the federal government. 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 concerning our product candidates 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. 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, or the Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. 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 post-grant review, *inter partes* review, and derivation proceedings.

Further, because of a lower evidentiary standard in these USPTO post-grant proceedings compared to the evidentiary standard in U.S. 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 our 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 our licensors' patent applications and the enforcement or defense of our or our 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. Consequently, if a third party that files a patent application in the USPTO before we file an application covering the same invention, the third party could therefore be awarded a patent covering an invention of ours or our 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 our 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 our 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 U.S. 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 U.S. Congress, the U.S. 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 our licensors' ability to obtain new patents and patents that we or our licensors might obtain in the future. For example, recent decisions raise questions regarding the award of patent term adjustment, or PTA, for patents where related patents have issued without PTA. Thus, it cannot be said with certainty how PTA will or will not be viewed in future and whether patent expiration dates may be impacted.

Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future. For example, the complexity and uncertainty of European patent laws have also increased in recent years. In Europe, a new unitary patent system took effect on June 1, 2023, which will significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, all European patents, including those issued prior to June 1, 2023, now by default automatically fall under the jurisdiction of a new European Unified Patent Court, or the UPC, for litigation involving such patents. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. 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 patents 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. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. We cannot predict how future decisions by the courts, the U.S. 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.

***We may become subject to claims challenging the inventorship or ownership of our or our 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 our 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. For example, we co-own a patent application with MedRx, which names inventors from our company and MedRx. It is possible that MedRx could challenge the inventorship of the individuals from our company. 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.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our 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.

***Patent terms may be inadequate to protect our competitive position on products or product candidates for a sufficient 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 U.S. 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. For example, issued patents covering the composition of ALTO-100 expired and patents covering the method of its manufacturing are due to expire in 2030; our composition of matter patents in ALTO-202 (compound) expired in May 2024 (in foreign countries) and are due to expire in 2026 (in the United States), and our polymorph composition of matter patents in ALTO-202 are due to expire in 2035; and patents covering the composition of ALTO-203 are due to expire in 2027, in all cases without taking into account patent term extensions or adjustments, and assuming payment of all applicable maintenance, renewal, and annuity fees. As a result, our owned and licensed 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 candidate, our business may be materially harmed.***

Depending upon the timing, duration, and specifics of any FDA marketing approval of any of our product candidates, one or more of our or our licensors' issued U.S. patents or issued U.S. 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, or 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 the EU Regulation (EC) No 469/2009 concerning the Supplementary Protection Certificate for medicinal products. 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.

***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 owned or licensed patents and patent applications. We rely on our outside counsel, third party vendors, or our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which 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.

***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 rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce, and any other elements of our discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. However, trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know-how, and if the license is not available on commercially-viable terms, then we may not be able to launch our product candidate.

Additionally, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. 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. Additionally, 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, whether inadvertently or through intentional acts of current or departing employees, or that competitors will not otherwise gain access to our trade secrets. If our trade secrets are not adequately protected, our business, financial condition, results of operations, and prospects could be adversely affected.

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

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, 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.

***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 or our licensors may in the future be subject to claims by former employees, consultants, or other third parties asserting an ownership right in our owned or licensed 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 owned or licensed 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.

**Risks Related to Our Reliance on Third Parties**

***We have relied and expect to continue to rely on third parties to conduct certain aspects of our 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.***

Although we rely on our internal, proprietary systems for data collection and our own clinical trial team to conduct our clinical trials (See "—We rely on, and intend to continue to rely on, our internal clinical development expertise to conduct our current and future clinical trials. This model includes internal teams and systems as well as external vendors and CROs to comprise a full clinical trial team. If our clinical trial team does not comply with applicable regulatory requirements, meet expected deadlines, or run trials effectively, our development programs and our ability to seek or obtain regulatory approval for or commercialize our product candidates may be delayed."), we rely or may rely in the future on third-party clinical investigators, medical institutions, and clinical data management organizations to conduct, supervise, and monitor

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 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 and harm our competitive position. As a result, delays may occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition, and prospects.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors, such as a failure to adhere to contractually obligated protocols regarding storing, packaging and distributing drug supplies, could delay clinical development or regulatory approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

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 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, or GLPs, and clinical trials are conducted in accordance with good clinical practices, or GCPs. 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 pre-approval inspections once an NDA is submitted to the FDA) of trial sponsors, clinical investigators, clinical trial sites, and IRBs. If we, our clinical trial sites, or other third parties fail to comply with applicable GLP, 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 before approving our marketing applications, if ever. 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 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.

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

If our 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, marketing approvals for our product candidates, and we may 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. Though we work to carefully manage our relationships with our third-party investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects. In addition, if an agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely.

***We 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 facilities for drug manufacturing, storage, distribution, or quality testing and have no current plans to develop our own clinical or commercial-scale manufacturing capabilities. We currently rely, and expect to continue to rely, on third-party contract developers and manufacturers to manufacture bulk drug substances, drug products, raw materials, samples, patch technology, components, and other materials for our product candidates and delivery devices, as well as for commercial manufacture if any of our product candidates receive regulatory approval. 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 clinical development product supplies will not be limited, interrupted, terminated, or will be of satisfactory quality or be available at acceptable prices. We typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements with any commercial manufacturer. There is no assurance that we will be able to timely secure needed supply arrangements on satisfactory terms, or at all. In addition, any replacement of our manufacturer could require significant effort and time because there may be a limited number of qualified replacements.

The manufacturing process for our product candidates is subject to the FDA's review and, in the future, may be subject to comparable foreign regulatory authority review. We, and our suppliers and manufacturers, some of which are currently our sole source of supply, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA and, in the future, comparable foreign regulatory authorities. 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, they will not be able to secure and/or maintain regulatory approval for the use of their manufacturing facilities. Moreover, we do not conduct the manufacturing process ourselves and are completely dependent on our CMOs for manufacturing our product candidates in compliance with cGMP. 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. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with applicable quality standards and regulations and guidelines; and we may be required to repeat some of the development program. The delays and costs associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget, or obtain regulatory approval for or market our product candidates.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce our 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 other ways, including:

- an inability to initiate or complete clinical trials of product candidates in a timely manner;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;

- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- loss of the cooperation of existing or future collaborators;
- requirements to cease development 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.

Reliance on third-party manufacturers entails additional risks such as limitations on supply availability resulting from capacity and scheduling constraints of third parties; the possible breach of manufacturing agreements by third parties because of factors beyond our control; the possible termination or non-renewal of the manufacturing agreements by the third party, at a time that is costly or inconvenient to us; failure to manufacture our product according to our schedule or at all; and the possible misappropriation of our proprietary information, including our trade secrets and know-how. Additionally, our CMOs may experience difficulties due to resource constraints or as a result of labor disputes, unstable political environments, or geopolitical tensions such as geopolitical tensions in China. If our CMOs were to encounter any of these difficulties, our ability to provide our product candidates to participants in clinical trials, or to provide product for treatment of patients if approved, would be jeopardized. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time consuming to implement, which would have a material adverse impact on our financial position.

***If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture product candidates may increase and commercialization may be delayed.***

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our products, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the output. The transition to larger scale production could prove difficult. In addition, if our third-party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

***We depend on sole source and limited source suppliers for certain drug substances, drug products, raw materials, samples, components, and other materials used in our product candidates. If we are unable to source these supplies on a timely basis, or establish 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.***

We depend on sole source and limited source suppliers for certain drug substances, drug products, raw materials, samples, components, and other materials used in our product candidates. For example, active pharmaceutical ingredients, or API, and drug product for ALTO-101 and ALTO-203 are manufactured by our supplier in China. We do not currently have long-term supply contracts with any of 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 in the future as we advance our clinical trials or commercialization plans, 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 utilize the drug products that we are required to purchase. Any change in our relationships with our CMOs or changes to contractual terms of our agreements with them could adversely affect our business, financial condition, results of operations, and prospects.

Furthermore, the climate of geopolitical tensions in China affecting global supply chains could impact our ability to continue to source API and drug product for ALTO-101 and ALTO-203 from our supplier in China. Certain Chinese biotechnology companies and CMOs may become subject to trade restrictions, sanctions, other regulatory requirements, or proposed legislation by the U.S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting the supply of material to us. Such restrictions could cause delays, disruptions, and cost

increases in our studies for ALTO-101 and ALTO-203 or have other adverse effects on the development of our product candidates and our business operations.

In addition, any of the sole source and 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 additional or replacement suppliers for these supplies, and obtaining regulatory clearance or approvals that may result from adding or replacing 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 sole source or 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 or sole 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.

***The operations of our suppliers that 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, some 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 (including tariffs proposed by the current administration);
- 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 as suggested by recent disclosure allegations against certain Chinese CMOs;
- disruptions in operations due to global, regional, or local public health crises or other emergencies or natural disasters;
- disruptions or delays in shipments; and
- changes in local economic conditions in countries where our manufacturers or suppliers are located.

In addition, certain Chinese biotechnology companies and CMOs may become subject to trade restrictions, sanctions, and other regulatory requirements by the U.S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting the supply of certain materials. 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.

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

Our product candidates are biopharmaceuticals and the process of manufacturing biopharmaceuticals is complex, time-consuming, highly regulated, and subject to multiple risks. Our CMOs must comply with legal requirements, including cGMPs, and guidelines for the manufacturing of biopharmaceuticals used in clinical trials and, if approved, marketed products. Our CMOs may have limited experience in the manufacturing of cGMP batches of our products.

Manufacturing biopharmaceuticals is highly susceptible to drug product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics, and difficulties in scaling the production process. If any such drug product loss occurs, the impact to our business could be compounded by the long lead times needed to procure additional drug product due to plant capacity limitations, or other restrictions, at our CMOs. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered at our third-party manufacturers' facilities, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely affect our business. Moreover, if the FDA or any other 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 approval until the deficiencies are corrected or we replace the manufacturer in our NDA with a manufacturer that is able to ensure compliance of the product being manufactured.

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

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

We cannot assure you that any stability or other issues relating to the manufacture of any of our current or future product candidates or products, if approved, will not occur in the future. If our third-party manufacturers were to encounter any of these difficulties, our ability to provide any product candidates to participants in clinical trials and products to participants, if approved, would be jeopardized. Any delay or interruption in clinical trial supplies could delay the completion of planned clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Any adverse developments affecting clinical or commercial manufacturing of our product candidates or products, if approved, may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our product candidates or products. We may also have to take inventory write-offs and incur other charges and expenses for product candidates or products, if approved, that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could adversely affect our business and delay or impede the development and commercialization of any of our product candidates or products, if approved, and could have an adverse effect on our business, financial condition, results of operations, and prospects.

As part of our process development efforts, we also may make changes to the manufacturing processes at various points during development, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate, or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our 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 and 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 candidate used in earlier clinical phases or at earlier portions of a trial to the product candidate used in later clinical phases or later portions of the trial.

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

We are currently party to license and collaboration agreements with parties such as Sanofi, MedRx, and Cerecor, and we expect to enter into similar strategic transactions in the future. We may have conflicts with our current or future collaborators, such as conflicts concerning the interpretation of preclinical or clinical data, the interpretation of a biomarker derived from our Platform, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations, or the ownership of intellectual property developed during our collaboration. Moreover, a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products. If any conflicts arise with any of our 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 additional collaborations; unwillingness by the 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. Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

***We have historically relied on an affiliated third party to provide certain business services and the replacement of such services could adversely affect our business operations.***

We engage a professional employment organization, or PEO, to provide us with payroll services, benefit services, and human resources support. As we continue to transition to operate as a standalone entity, we intend to hire additional qualified personnel to provide certain of these functions internally in the future. Upon the termination of the PEO relationship, such services will be provided internally or by unaffiliated third parties, and we expect that in some instances, we will incur higher costs to obtain such services than we incurred under the terms of such agreement.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we currently rely on third parties to manufacture our product candidates and to perform quality testing, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements, and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are intentionally or inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets and despite our efforts to protect our trade secrets, a competitor's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations, and prospects.

**Risks Related to Government Regulation**

***Our relationships with healthcare providers and physicians and third-party payors may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Our current and future arrangements with healthcare providers, third-party payors, and customers can expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, and if approved, sell, market, and distribute our products. In particular, the research of our product candidates, as well as

the promotion, sales, and marketing of our product candidates is subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring, and commission(s), certain customer incentive programs, and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The applicable federal, state, and foreign healthcare laws and regulations laws that may affect our ability to operate now or in the future include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering, or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, or recommendation of any good, facility, item, or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other;
- the federal civil and criminal false claims laws, including the federal FCA which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government healthcare programs if they are deemed to "cause" the submission of false or fraudulent claims. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- HIPAA which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (*e.g.*, public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact, or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating the health care fraud statute under HIPAA without actual knowledge of the statute or specific intent to violate it;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy and security of individually identifiable health information of covered entities subject to the rule, including health plans, healthcare clearinghouses and certain healthcare providers and their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information for or on their behalf, as well as their covered subcontractors;
- the federal Physician Payments Sunshine Act and its implementing regulations, which require some manufacturers of drugs, devices, biologicals, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (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;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to claims involving healthcare items or services reimbursed by non-governmental third-party

payors, including private insurers, and may be broader in scope than their federal equivalents; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state and local laws that require the registration of pharmaceutical sales representatives; and state laws that protect consumer privacy or require notice to customers about how personal information is used and collected. Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage, and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal, state, and foreign enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, significant fines and penalties, and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and may divert our management's attention from the operation of our business.

It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal, and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from participation in federal and state funded healthcare programs, contractual damages, and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Any action for violation of these laws, even if successfully defended, could cause us to incur significant legal expenses and divert management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future marketed products could adversely affect our business, results of operations, and financial condition.

***Drug marketing and reimbursement regulations in the EU may materially affect our ability to market and receive coverage for our products in the EU member states.***

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

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians and other healthcare professionals to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is also prohibited in the EU. Interactions between pharmaceutical companies and healthcare professionals are governed by the national anti-bribery laws of EU member states, national sunshine rules, regulations, industry codes of conduct, any physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties substantial fines and imprisonment.

Payments made to healthcare professionals, healthcare organizations, students, or patient organizations in EU member states must increasingly be publicly disclosed. Moreover, agreements with healthcare professionals must be the subject of a

prior written agreement between the parties and often must be the subject of prior notification and/or approval by the healthcare professional's employer, his or her competent professional organization, and/or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, or fines.

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

Many EU Member States also periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. 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 Health Technology Assessment ("HTA") 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 Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. This regulation, which began to apply on January 12, 2025, through a phased implementation, is intended to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period. 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. Entry into application of the HTA regulation is anticipated to increase reliance by competent national authorities on reference pricing mechanisms, the mechanism whereby countries reflect the reimbursement price in other EU member states. This has the potential to result in a decrease in reimbursement price in a number of EU member states to reflect the price fixed in the EU member state with the lowest reimbursement price.

***Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.***

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

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs or similar regulations. As such, we and our contract manufacturers will be subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities to assess compliance with cGMPs or similar requirements and adherence to commitments made in any NDA, other marketing application, and previous responses to inspection

observations. Accordingly, we and others with which we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, and such approvals may be subject to significant limitations on the approved indicated uses for which the product may be marketed (e.g., use restrictions for specified age groups, warnings, precautions or contraindications), and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS program as a condition of approval of our product candidates or similar risk management measures, which could entail requirements for long-term patient follow-up, a medication guide, physician training and communication plans, or additional elements to ensure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools.

The FDA or comparable foreign regulatory authorities may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, such as adverse events of unanticipated severity or frequency, or problems with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on that product, the manufacturing facility or us, including revisions to the approved labeling to add new safety information or a "black box" warning, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters, or holds on clinical trials;
- refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications submitted by us or suspension or revocation of approvals;
- product seizure or detention or refusal to permit the import or export of our products; and
- injunctions 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.

Additional health reform measures may continue and affect our business in unknown ways, particularly given the recent change in presidential administration. The current administration is pursuing policies to reduce regulations and expenditures across the U.S. government including at FDA and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. The policies of the FDA and comparable regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. For example, the U.S. Supreme Court's June 2024 decision in *Loper Bright Enterprises v. Raimondo* overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The *Loper* decision could result in additional legal challenges to regulations and decisions issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the *Loper* decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature, or extent of government regulation that may arise from current or future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and our business, results of operations, and financial condition could be adversely affected.

***The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.***

The FDA and comparable foreign regulatory authorities strictly regulate marketing, labeling, advertising, and promotion of prescription drugs. These regulations include standards and restrictions for direct-to-consumer advertising, industry-

sponsored scientific and educational activities, promotional activities involving the internet, and off-label promotion. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. While physicians in the United States may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote any products will be narrowly limited to those indications that are specifically approved by the FDA.

If we are found to have promoted such off-label uses, we may become subject to significant liability. 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. If we cannot successfully manage the promotion of any product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business, results of operations, and financial condition.

***Ongoing healthcare legislative and regulatory reform measures may adversely affect our business, results of operations, and financial condition.***

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA, as amended by the Health Care and Education Reconciliation Act of 2010, was passed by Congress, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. Since its enactment, certain provisions the ACA have been subject to executive, judicial, and congressional challenges and amendments. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or the IRA, was enacted, which among other things extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and by creating a newly established manufacturer discount program. It is unclear how healthcare reform measures of the current administration will impact our business.

In addition, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs covered under Medicare that have been on the market for at least seven years and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. On August 15, 2024, HHS announced the agreed-upon prices for the first ten drugs that were subject to price negotiations, although the drug price negotiation program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional drugs covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare drug price negotiation program. Further, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.

Further, 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.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

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

The ability and propensity 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 and comparable foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, social movements promoting alternatives to the use of drugs to treat certain neuropsychiatric conditions, and other events that may otherwise affect the FDA's and comparable foreign regulatory authorities' performance of routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. Moreover, the current administration is pursuing policies to reduce expenditures across the U.S. government which may include directives to reduce agency workforce, including at the FDA. Such policy changes could create additional uncertainty for our business if key personnel are not in place to support the review, approval, and commercialization of our products.

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 and funding of the U.S. Department of Veterans Affairs, which we partner with for certain clinical trials, the FDA, and other national and foreign authorities may reduce resources, increase internal costs incurred to counteract the potential reduction in resources, and slow the time necessary for review and/or approval by necessary government 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 agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities and the federal government may, from time to time, operate under a continuing resolution that could result in a shutdown if Congress is unable to timely pass an appropriations bill. If a prolonged government shutdown occurs, or if global health concerns continue to 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.

***We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards, and other requirements could adversely affect our business, results of operations, and financial condition.***

We maintain a large quantity of sensitive information, including confidential business and health-related information in connection with the conduct of our clinical trials, and personal information related to our employees, and we are subject to laws and regulations governing the privacy and security of such information. In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure, and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect, and in certain cases has affected, our business and is expected to increase our compliance costs and exposure to liability.

In the United States, numerous federal and state laws and regulations apply to our operations or the operations of our partners, including state and federal data breach notification laws, state health information privacy laws and federal and state consumer protection laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal information. Among these regulations are: Section 5 of the Federal Trade Commission Act, which prohibits unfair or deceptive commercial practices; and HIPAA, as amended by HITECH, and the regulations promulgated thereunder. We may obtain health information from third parties, including information submitted by potential clinical trial participants through our internal, proprietary systems for data collection that are subject to privacy and security requirements under 21 CFR Part 11 governing the electronic storage of records that are required by the FDA's regulations to be maintained or submitted to the FDA. Actual or perceived failure to comply with any such law or regulation by either us or our third-party vendors could adversely affect our business, results of operations, and financial condition.

In addition, numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights

concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018, or CCPA, applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with, data breach litigation. Similar comprehensive privacy laws have been enacted and are continuing to be proposed in numerous other states and at the federal level reflecting a trend toward more stringent privacy legislation in the United States.

In addition, several states have enacted laws that provide additional protection to consumer health data such as the state of Washington, which enacted a comprehensive privacy bill, called the My Health My Data Act, which broadly defines consumer health data, places restrictions on processing consumer health data (including imposing stringent requirements for consents), provides consumers certain rights with respect to their health data, and creates a private right of action to allow individuals to sue for violations of the law. Other states are considering and may adopt similar laws. While certain of these laws, such as the CCPA, exempt data regulated by HIPAA and certain clinical trial data, if passed and applicable to us, these laws may add additional complexity to our existing compliance obligations and may require us to modify our policies and practices and may increase our potential liability and adversely affect our business.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data privacy and security. For example, the EU's General Data Protection Regulation ("EU GDPR") and the United Kingdom's GDPR ("UK GDPR") (collectively, "GDPR") impose strict requirements for processing personal data. Under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros under the EU GDPR, 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual global revenue, whichever is greater; or 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.

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

In the ordinary course of business, we have transferred, and may in the future transfer, personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA) and the United Kingdom (UK) have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt or have already adopted similarly stringent data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

In addition to data privacy and security laws, we are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We publish privacy policies and other statements concerning data privacy and security. Regulators in the United States are increasingly scrutinizing these statements, and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition, and results of operations. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly.

Obligations related to data privacy and security (and consumers' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. With the CCPA, and other laws, regulations, and other obligations relating to privacy and data protection imposing new and relatively burdensome obligations, and with the substantial uncertainty over the interpretation and application of these and other obligations, we may face challenges in addressing their requirements and making necessary changes to our policies and practices and may incur significant costs and expenses in an effort to do so. Additionally, if third parties with which we work, such as vendors or service providers, violate applicable laws, rules, or regulations or our policies, such violations may also put our or our clinical trial and employee data, including personal data, at risk, which could in turn have an adverse effect on our business.

If we or the third parties with whom we work fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims) and mass arbitration demands; additional reporting requirements and/or oversight; bans or restrictions on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. 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. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials); inability to process personal data 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.

***Additional laws and regulations governing international operations could adversely affect our business, results of operations and financial condition.***

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment, or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate, and other related parties for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations, and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing,

or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our research and development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

***We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.***

We are subject to U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws. Among other things, Trade Laws prohibit companies and their employees, agents, clinical research organizations, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government authorities or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase over time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals, and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

**Risks Related to Ownership of Our Common Stock and Our Status as a Public Company**

***An active and liquid trading market for our common stock may not continue to develop or be sustained.***

Prior to the IPO, there was no public market for our common stock. Although our common stock is listed on The New York Stock Exchange, an active trading market for our shares may not continue to develop or be sustained. If an active trading market for our common stock does not continue developing or is not sustained, you may not be able to sell your shares at an attractive price or at all. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock in the future, 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 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 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 ALTO-100, ALTO-300, ALTO-101, ALTO-203, and our other product candidates or future development programs;
- results and timing of preclinical studies and ongoing and future clinical trials, or the addition, suspension, or termination of any such clinical trials;
- the timing of payments we may make or receive under existing license and collaboration arrangements or the termination or modification thereof;
- our execution of any strategic transactions, including 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 any of our product candidates receives 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;
- global or regional public health emergencies, natural disasters, or major catastrophic events;
- adverse macroeconomic conditions or geopolitical events, including, the conflict between Ukraine and Russia, the conflict in the Middle East, geopolitical tensions in China, high levels of inflation, fluctuating interest rates, and proposed tariffs;
- the impacts of inflation and rising interest rates on our business and operations; and
- changes in general market and economic conditions.

If our quarterly or annual operating results 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 may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of shares of our common stock.***

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

- volatility and instability in the financial and capital markets;
- adverse macroeconomic conditions or geopolitical events, including the conflict between Ukraine and Russia, the regional conflict in the Middle East, geopolitical tensions in China, high levels of inflation, fluctuating interest rates, and proposed tariffs;
- announcements relating to our product candidates, including the results of clinical trials by us or our collaborators, such as our announcement regarding our Phase 2b trial of ALTO-100 in MDD in October 2024;
- announcements by competitors that impact our competitive outlook;
- negative developments with respect to our Platform, 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 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;
- expiration of market standoff or lock-up agreements;

- conditions and trends in the pharmaceutical, biotechnology, and other industries;
- recruitment and departures of key personnel;
- regulatory developments within, and outside of, the United States, including changes in the structure of health care payment systems;
- litigation or arbitration;
- 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.

***We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.***

We currently anticipate that we will retain future earnings for the research, development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. The Amended Loan Agreement and the Convertible Grant Agreement contain, and any future debt or other financing arrangements may contain, terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders therefore will be limited to the appreciation in the price of our common stock.

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

As of March 1, 2025, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially held, in the aggregate, approximately 35% of our outstanding common stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. For example, these stockholders would be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This level of control may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The 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.

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

We are an "emerging growth company" as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (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 this Annual Report and our future 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 could be an emerging growth company for up to five years following the year in which we completed the IPO, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of the IPO, (b) in which we have total annual gross revenue of at least $1.235 billion and (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. Investors may find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies also can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption, and, as a result,

our operating results and financial statements may not be comparable to the operating results and financial statements of companies who have adopted the new or revised accounting standards.

We also are a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter. 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 Form10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

***Conflicts of interest may arise because some members of our board of directors are representatives of our principal stockholders.***

Certain of our principal stockholders or their affiliates are venture capital funds or other investment vehicles that could invest in entities that directly or indirectly compete with us. As a result of these relationships, when conflicts arise between the interests of the principal stockholders or their affiliates and the interests of other stockholders, members of our board of directors that are representatives of the principal stockholders may not be disinterested.

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

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

As of March 17, 2025, we had outstanding 27,072,129 shares of common stock. Of these shares, substantially all of the 9,246,000 shares sold in the IPO (excluding any shares sold in the directed share program implemented in connection with the IPO) are freely tradable and, subject to the restrictions of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, substantially all of our additional shares of common stock became available for sale in the public market on July 30, 2024, which was 180 days after the date of the final prospectus filed in connection the IPO, following the expiration of lock-up agreements between some of our stockholders and the underwriters and/or market stand-off provisions. In addition, we filed a registration statement on Form S-8 under the Securities Act registering the issuance of 5,721,134 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under the registration statement on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, and the restrictions of Rule 144 in the case of our affiliates. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Additionally, the holders of 2,032,595 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act as provided under the terms of our amended and restated investors' rights agreement between us and various of our stockholders, subject to the restrictions described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

***We have broad discretion in the use of our cash and cash equivalents and may not use them effectively, which could affect our results of operations and cause our stock price to decline.***

Our management has considerable discretion in the application of our cash and cash equivalents, including the net proceeds from the IPO. We may use our cash and cash equivalents for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

***Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of our company more difficult, limit attempts by our stockholders to replace or remove our current management, and limit the market price of our common stock.***

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may have the effect of delaying or preventing a change of control or changes in our board of directors and management. Our amended and restated certificate of incorporation and amended and restated bylaws includes provisions that:

- authorize our board of directors to issue, without further action by the stockholders, shares of undesignated preferred stock with terms, rights, and preferences determined by our board of directors that may be senior to our common stock;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- specify that special meetings of our stockholders can be called only by directors representing a majority of the total authorized size of our board of directors, the chairperson of our board of directors, or our chief executive officer;
- establish an advance notice procedure for stockholder proposals to be brought before an annual meeting, including proposed nominations of persons for election to our board of directors;
- establish that our board of directors is divided into three classes, with each class serving three-year staggered terms;
- prohibit cumulative voting in the election of directors, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose;
- provide that our directors may be removed for cause only upon the vote of at least 66 2/3% of our outstanding shares of voting stock;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum; and
- require the approval of our board of directors or the holders of at least 66 2/3% of our outstanding shares of voting stock to amend our bylaws and certain provisions of our certificate of incorporation.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which generally, subject to certain exceptions, prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder. Any of the foregoing provisions could limit the price that investors might be willing to pay in the future for shares of our common stock, and they could deter potential acquirers of our company, thereby reducing the likelihood that holders of our common stock would receive a premium for their shares of our common stock in an acquisition.

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

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- 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 under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws;
- any action seeking to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation, or our amended and restated bylaws;

- any action to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. Additionally, investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation will further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid and several state trial courts have enforced such provisions and required that suits asserting Securities Act claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions and a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and the provisions may not be enforced by a court in those other jurisdictions. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with litigating Securities Act claims in state court, or both state and federal court, which could seriously harm our business, results of operations, and financial condition.

This exclusive forum provision may result in increased costs to stockholders to bring a claim. Further, this exclusive 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 our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

**General Risk Factors**

***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 significant 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 federal gross net operating loss, or NOL, carryforwards of $42.2 million and state gross NOL carryforwards of $33.6 million. Portions of these NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Internal Revenue Code of 1986, as amended, or the Code, federal NOL carryforwards arising in taxable years beginning after December 31, 2017 will not expire and may be carried forward indefinitely, but the deductibility of such federal NOL carryforwards in a taxable year is limited to no more than 80% of taxable income in such year (with certain adjustments).

In addition, under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and certain other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. These ownership changes may limit the amount of NOL and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. We completed a study to assess whether an ownership change has occurred through December 31, 2024. Based on these analyses, an ownership change was identified in 2019, 2021 and 2023 as a result of the completion of certain preferred stock financings. As a result of the ownership shifts that have occurred, we determined that $24.0 million of our gross federal NOLs and tax credit carryforwards are subject to an annual utilization limitation, which can be increased in the five year period post change date for any realized built-in gain. Such limitations expire no later than December 31, 2029 and the related gross federal NOLs and tax credit carryforwards are subject to a full valuation allowance as of December 31, 2024. We will continue to monitor equity movement and its impact on the utilization of the NOLs and credits as we could experience additional ownership changes subsequent to December 31, 2024, which may result in additional limitations on the utilization of NOL carryforwards and credits. 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. 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. As a result of the foregoing, we have a full valuation allowance for deferred tax assets, including our NOL carryforwards.

In addition, we have received, and may receive, research and development tax credits in certain jurisdictions, including Australia, from time to time. To the extent such tax credits are reduced or eliminated or we no longer qualify for such tax credits in the future, our ability to offset our taxable income or taxes in such jurisdictions will be limited.

***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 Tax Cuts and 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. For example, the Tax Cuts and Jobs Act requires the capitalization and amortization of certain research and experimental expenses over five years if incurred in the United States and fifteen years if incurred outside the United States, rather than deducting such expenses currently. Although there have been legislative proposals to repeal or defer the capitalization requirement, there can be no assurance that such requirement will be repealed, deferred, or otherwise modified. 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.

***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, bank failures, 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 Russia-Ukraine conflict, conflict in the Middle East, and geopolitical tensions in China). The financial institutions in which we hold our cash and cash equivalents are also subject to risk of failure. Any such loss or limitation on our cash and cash equivalents would adversely affect our business.

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 will be 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 clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline.

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

As a public company, and particularly after we are no longer an emerging growth company, we will 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 New York Stock Exchange 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 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. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees, or as executive officers. 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.***

As a public company, we are required to comply with the SEC's rules implementing Sections 302 and 404 of the Sarbanes-Oxley Act, which will require 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. However, as an emerging growth company, our independent registered public accounting firm will not be required to formally 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. When we lose our status as an "emerging growth company" and reach an accelerated filer threshold, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for our management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we may need to upgrade our information technology systems; implement additional financial and management controls, reporting systems, and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

There may be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its Section 404 reviews, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the New York Stock Exchange, the SEC, or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

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

As a public company, 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 and /or close 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, and has been volatile following our announcement regarding our Phase 2b trial of ALTO-100 in MDD in October 2024. The stock market in general, and the New York Stock Exchange 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, 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.**

Not applicable.

**Item 1C. Cybersecurity.**

***Risk Management and Strategy***

We have implemented and maintain various information security processes designed to identify, assess, and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature, employee personal information, and clinical trial data, or Information Systems and Data.

Our Senior Director, Information Technology, in conjunction with a third party service provider, under the direction of our Chief Financial Officer, or CFO, help management identify, assess and manage our cybersecurity threats and risks. With the assistance of our Senior Director, Information Technology and third-party service provider, we identify and assess risks from cybersecurity threats by monitoring and evaluating our threat environment and our risk profile using various methods including, for example, automated tools for ransomware and virus protection, identity verification tools aimed at ensuring authorized environment access, and ongoing vulnerability assessments.

Depending on the environment and system, we implement and maintain various technical, physical, and organizational measures and processes designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: data encryption for certain data, network security controls, data segregation for certain data, access controls, physical security controls, monitoring for certain systems, asset management and tracking, and employee training. We also maintain cybersecurity insurance.

Our assessment and management of material risks from cybersecurity threats are taken into account in our overall risk management processes. For example, we evaluate certain identified material risks from cybersecurity threats against our overall business objectives and will report material risks, if identified, to the audit committee of the board of directors, which evaluates our overall enterprise risk.

We use third-party service providers to assist management to identify, assess, and manage material risks from cybersecurity threats, including for example, a managed security provider and professional services firms, including outside legal counsel.

We use third-party service providers to perform a variety of functions throughout our business, including, for example, application providers, hosting companies, contract research organizations, and contract manufacturing organizations. We have certain vendor management processes to help manage cybersecurity risks associated with our use of certain of these providers, and, depending on the nature of the services provided, the sensitivity of the Information Systems and Data at

issue, and the identity of the provider, those processes may involve different levels of assessment and risk mitigation measures, including, for example, the imposition of contractual obligations related to cybersecurity on the provider.

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see the sections titled: "Risk Factors—Risks Related to our Business and Operations—If our telecommunications or information technology systems, or those used by our collaborators, CROs, CMOs, clinical sites, third-party logistics providers, distributors, or other contractors, consultants, or third party service providers upon which we rely, are or were compromised, become unavailable, or suffer security breaches, loss, or leakage of data or other disruptions, we could suffer adverse consequences resulting from such compromise, including but not limited to, operational or service interruption, harm to our reputation, litigation, fines, penalties and liability, compromise of sensitive information related our business, and other adverse consequences." and "Risk Factors—Risks Related to Government Regulations—We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards, and other requirements could adversely affect our business, results of operations, and financial condition."

***Governance***

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

Our cybersecurity risk assessment and management processes are implemented and maintained by certain members of Company management, including our CFO, leveraging the expertise of our Senior Director, Information Technology and third party service provider. Our CFO has three years of oversight responsibilities for cybersecurity elements and has been involved in the oversight of the implementation of the Company's current cybersecurity measures. Our Senior Director, Information Technology has approximately 20 years of oversight responsibilities for cybersecurity elements and has been involved in the oversight of the implementation of the Company's current cybersecurity measures.

Currently, our CFO and Senior Director, Information Technology are collectively responsible for hiring appropriate personnel, managing external third-party providers, helping to integrate cybersecurity risk considerations into our overall risk management strategy, communicating key priorities to relevant personnel, approving budgets, helping prepare for cybersecurity incidents, approving cybersecurity processes, and reviewing security assessments and other security-related reports.

Our cybersecurity incident response processes are designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including to our CFO. Senior Director, Information Technology, and General Counsel. As part of those processes, members of management, including our Senior Director, Information Technology and CFO, would work to help the Company mitigate and remediate cybersecurity incidents of which they are notified. In addition, our incident response processes are designed to report certain cybersecurity incidents to the audit committee of the board of directors.

The audit committee receives periodic reports from management concerning our cybersecurity risks and the processes we have implemented to address them. The audit committee also has access to various reports, summaries or presentations related to cybersecurity threats, risk and mitigation.

**Item 2. Properties.**

Our principal office is located at 650 Castro Street, Suite 450, Mountain View, CA 94041, where we lease 16,332 square feet of office space in a multi-tenant building under a lease with an initial lease term of 65 months that terminates in March 2030 with an option to extend up to an additional three years. We also have a one-time option to terminate the lease after the third lease year. We believe that our existing facility is adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

**Item 3. Legal Proceedings.**

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm.

**Item 4. Mine Safety Disclosures.**

Not applicable.

## Part II

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

On February 2, 2024, our common stock began trading on the New York Stock Exchange under the symbol “ANRO”.

**Stockholders**

As of March 1, 2025, there were 30 stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Unregistered Sales of Equity Securities**

None

**Use of Proceeds from Public Offering of Common Stock**

On February 1, 2024, our Registration Statement on Form S-1, as amended (File No. 333-276495), or the IPO Registration Statement, was declared effective. On February 6, 2024, we closed the IPO and 9,246,000 shares of our common stock were issued and sold at a public offering price of $16.00 per share, inclusive of the exercise in full by the underwriters of their option to purchase up to an additional 1,206,000 shares of common stock. Jefferies LLC, Cowen and Company, LLC, Stifel, Nicolaus & Company, Incorporated and William Blair & Company, L.L.C. acted as joint lead book-running managers and Robert W. Baird & Co. Incorporated acted as lead manager for the offering.

The aggregate net proceeds from the IPO, after underwriting discounts and commissions, and other offering expenses of $4.6 million, were $133.0 million. There has been no material change in the planned use of proceeds from our IPO as described in our prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on February 5, 2024.

**Dividend Policy**

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, to support our operations and finance the growth and development of our business. We have no present intention to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions (including any restrictions in our then-existing debt arrangements), business prospects, and other factors our board of directors may deem relevant, and subject to the restrictions contained in any future financing instruments. In addition, the terms of our Amended Loan Agreement with K2 HealthVentures and the terms of our Convertible Grant Agreement with Wellcome restrict our ability to pay dividends. Investors should not purchase our common stock with the expectation of receiving cash dividends.

**Issuer Purchases of Equity Securities**

None.

### Item 6. [ Reserved ]

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

*You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes included elsewhere in this Annual Report.*

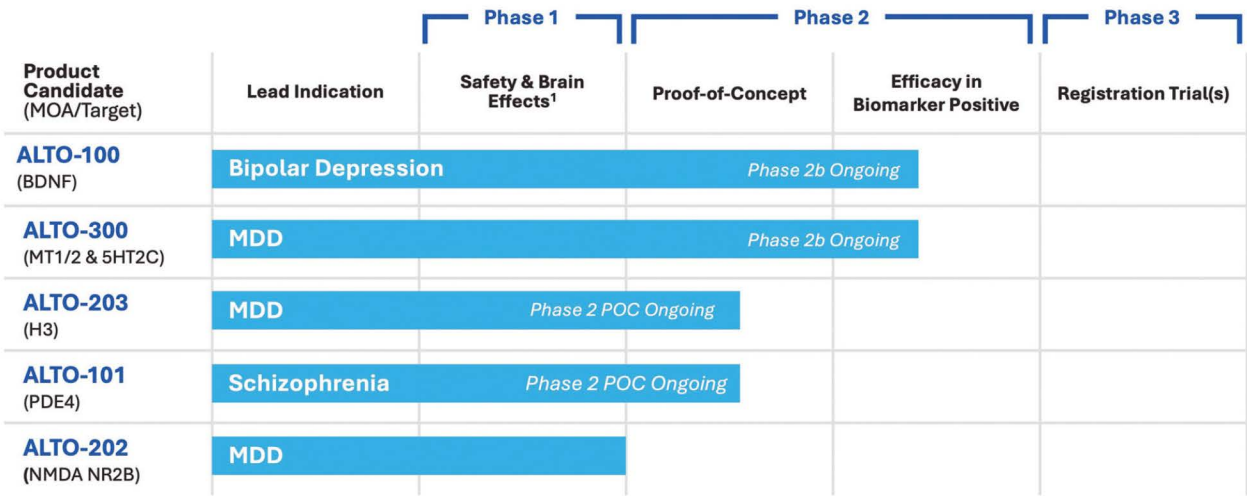
*As discussed in the section titled "Special Note Regarding Forward Looking Statements," the following discussion and analysis includes forward-looking statements that involve risks and uncertainties. Our actual results and the timing of selected events could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to those identified below and those set forth in the section titled "Risk Factors" under Part I, Item 1A.*

**Overview**

We are a clinical-stage biopharmaceutical company with a mission to redefine psychiatry by leveraging neurobiology to develop personalized and highly effective treatment options. Through insights derived from our scalable and proprietary Platform, we aim to discover brain-based biomarkers to better identify which patients are more likely to respond to our novel product candidates. Our current pipeline consists of five clinical-stage assets addressing high-need therapeutic areas, including MDD, BPD, and schizophrenia. Our most advanced programs are supported by prospectively replicated evidence of clinical activity in biomarker-characterized populations.

Our clinical-stage product candidates are being advanced based on extensive preclinical and clinical data that suggest the potential to bring significant improvements to patient populations not adequately treated with current standard-of-care medications.

Our pipeline of clinical-stage product candidates is depicted below:




**BDNF: Brain Derived Neurotrophic Factor; MDD: Major Depressive Disorder; MT1/2: Melatonin Receptor 1 and 2; 5-HT2C: 5-Hydroxytriptamine Receptor 2C; H3: Histamine H3 Receptor; PDE4: Phosphodiesterase-4; NMDA NR2B: N-methyl-D-aspartate Receptor Subtype 2B**

[1]We have active investigational new drug applications, or INDs, for each of ALTO-100, ALTO-300, ALTO-203, ALTO-101, and ALTO-202 in the indications listed. ALTO-100, ALTO-203, ALTO-101, and ALTO-202 were evaluated in Phase 1 safety trials by their respective originators prior to our acquisition or licensing of the product candidate.

Since our inception in 2019, we have devoted substantially all of our resources to the research and development of our product candidates by conducting clinical trials and preclinical studies, building our Precision Psychiatry Platform, and recruiting management and technical staff to support these operations. To date, we have funded our operations primarily through the aggregate net proceeds from equity financings (including from our IPO and pre-IPO sales of our convertible preferred stock) and borrowings under our loan and security agreement.

We have not generated any revenue from product sales and we have incurred recurring losses since our inception. Our net losses were $61.4 million and $36.3 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $138.4 million. We expect to continue to generate operating losses

and negative operating cash flows for the foreseeable future. We anticipate that our operating expenses and capital expenditures will increase substantially with our ongoing activities, particularly as we:

- continue to progress the clinical development of our product candidates, including ALTO-100 and ALTO-300 in ongoing Phase 2b clinical trials and potential Phase 3 programs;
- advance additional product candidates through clinical development;
- require the manufacture of larger quantities of our product candidates to support future clinical trials or potential commercialization;
- seek marketing authorizations for any of our product candidates that successfully complete clinical development, if any;
- acquire or license other product candidates or technologies;
- make milestone, royalty, or other payments under any current or future license agreements;
- obtain, maintain, protect, and enforce our intellectual property portfolio;
- seek to attract and retain new and existing skilled personnel; and
- add operational, legal, financial and management information systems and personnel to support our product development and clinical execution, as well as to support our transition to a public company.

We will not generate any revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our product candidates. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing, and distribution.

As a result, we will need substantial additional funding to support our operating activities as we advance our product candidates through clinical development, seek regulatory approval, and prepare for and, if any of our product candidates are approved, proceed to commercialization. Until such time, if ever, as we can generate substantial revenue from product sales to support our cost structure, we expect to finance our operating activities through a combination of public or private sales of equity, government or private party grants, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms, or at all.

If we are unable to obtain funding, we will be forced to delay, reduce, or eliminate some or all of our research and development programs, product portfolio expansion, or commercialization efforts, which could adversely affect our business prospects, or we may be unable to continue operations. Although we continue to pursue these plans, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all.

As of December 31, 2024, we had cash, cash equivalents, and restricted cash of $168.7 million. In February 2024, we raised net proceeds of approximately $133.0 million in our IPO. We believe that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements into 2028. See "—Liquidity and Capital Resources."

**License and Other Agreements**

For a detailed description of our license, collaboration and other agreements, see "Item 1. Business—License and Other Agreements" in this Annual Report.

## Components of Results of Operations

### *Operating Expenses*

*Research and Development Expenses*

Research and development expenses consist primarily of costs incurred for the development of our product candidates and our platform and technology building efforts, which include:

- personnel expenses, including salaries, benefits, and stock-based compensation expense for our employees engaged in research and development functions;
- expenses incurred in connection with the clinical development of our product candidates, including under agreements with clinical sites and CROs;
- fees incurred in connection with license agreements and asset acquisitions;
- costs of manufacturing drug product and drug supply related to our current or future product candidates;
- cost of outside consultants engaged in research and development functions;
- expenses related to regulatory affairs; and
- fees for maintaining licenses and other amounts due under our third-party licensing agreements.

We expense research and development costs in the periods in which they are incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks, using information provided to us by our vendors and analyzing the progress of our clinical trials or other services performed. Significant judgment and estimates are made in determining the accrued expense balances at the end of any reporting period.

Research and development activities are central to our business model. We expect our research and development expenses to increase substantially for the foreseeable future as we advance our product candidates into and through later stage clinical trials, pursue regulatory approval of our product candidates, build our operational and commercial capabilities for supplying and 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 costly and time-consuming. Furthermore, product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. 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, conduct of clinical trials, investment in our clinical programs, competition, manufacturing capability, and commercial viability. We may never succeed in achieving 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 applicable regulatory authorities.

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

- the timing and progress of our clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the amount and timing of any milestone payment due under an existing, or any future, license or collaboration agreement or asset acquisition;
- 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 in our clinical trials;
- patient drop-out or discontinuation rates;
- potential additional safety monitoring requested by regulatory authorities;

- the phase of development of our product candidates;
- the efficacy and safety profile of our product candidates;
- the timing, receipt, and terms of any approvals from applicable regulatory authorities including the FDA and non-U.S. regulators;
- 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 also expect to incur significant manufacturing costs as our CMOs develop scaled commercial manufacturing processes. However, we do not believe that it is possible at this time to accurately project expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

*General and Administrative Expenses*

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development, and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, information technology, auditing, tax and consulting services, travel expenses, and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we expand our headcount to support our continued research and development of our product candidates. We also expect to incur increased expenses associated with operating as a public company, including costs related to accounting, audit, legal, regulatory, and tax-related services, costs related to compliance with the rules and regulations of the SEC and listing standards applicable to companies listed on a national securities exchange, director and officer insurance costs, and investor relations costs. In addition, if we obtain regulatory approval for any of our product candidates and do not enter into a third-party commercialization collaboration, we expect to incur significant expenses related to building a sales and marketing team to support product sales, marketing, and distribution activities.

***Other Income (Expense)***

Other income (expense) consists primarily of interest income on our cash and cash equivalents, interest expense on borrowings under our loan and security agreement, and non-cash changes in the fair value of our Convertible Grant Agreement and our preferred stock warrant liability.

**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:

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| | (in thousands) | |
| Operating expenses: | | |
| Research and development | $ 46,996 | $ 30,291 |
| General and administrative | 21,614 | 7,518 |
| Total operating expenses | 68,610 | 37,809 |
| Loss from operations | (68,610) | (37,809) |
| Other income (expense): | | |
| Interest income | 8,851 | 2,349 |
| Interest expense | (1,375) | (1,370) |
| Other, net | (297) | 525 |
| Total other income, net | 7,179 | 1,504 |
| Net loss | $ (61,431) | $ (36,305) |

*Research and Development Expenses*

The following table summarizes our research and development expenses by program for the periods presented:

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| | (in thousands) | |
| Direct external program expenses: | | |
| ALTO-100 | $ 7,371 | $ 7,748 |
| ALTO-300 | 6,410 | 3,070 |
| ALTO-203 | 3,672 | 222 |
| ALTO-101 | 2,798 | 1,731 |
| Other clinical development | 1,622 | 1,593 |
| Licenses | 2,064 | 320 |
| Internal and unallocated expenses: | | |
| Personnel-related costs | 18,935 | 13,133 |
| Other unallocated expenses | 4,124 | 2,474 |
| Total research and development expenses | $ 46,996 | $ 30,291 |

Research and development expenses were $47.0 million for the year ended December 31, 2024, compared to $30.3 million for the year ended December 31, 2023. The increase of $16.7 million was primarily due to the following:

- an increase of approximately $3.3 million related to our ongoing ALTO-300 Phase 2b clinical trial, which began in 2023, and an increase of $4.5 million related to our ALTO-203 and ALTO-101 Phase 2 POC clinical trials, which began in 2024;
- an increase of approximately $2.0 million related to development milestones achieved under licensing agreements covering ALTO-203 and ALTO-101; and
- an increase of approximately $5.8 million in salary and personnel related costs, which includes $1.5 million of non-cash stock based compensation.

*General and Administrative Expenses*

General and administrative expenses were $21.6 million for the year ended December 31, 2024, compared to $7.5 million for the year ended December 31, 2023. The increase of $14.1 million during 2024 was primarily due to the following:

- an increase of approximately $6.4 million in salary and personnel related costs, which includes $3.3 million of non-cash stock-based compensation; and
- an increase of approximately $8.2 million in consulting fees and professional fees and other expenses related to being a publicly traded company.

*Other Income (Expense)*

Other income, net was $7.2 million for the year ended December 31, 2024, compared to $1.5 million for the year ended December 31, 2023. The increase in Other income, net of $5.7 million was primarily due to the increase in interest income of $6.5 million in the year ended December 31, 2024 compared to the year ended December 31, 2023. The increase in interest income was partially offset by an increase in expense related to changes in fair value of $0.8 million, driven primarily by expenses related to changes in the fair value of our warrant liability in 2024, compared to income related to changes in the fair value of our warrant liability in 2023.

**Liquidity and Capital Resources**

We have incurred net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. We have not yet commercialized any of our product candidates, which are in various phases of development, and we do not expect to generate revenue from sales of any of our product candidates for several years, if at all. As we progress through the phases of development, we anticipate that we will incur increasing losses in future quarters and years compared to historical periods. To date, we have funded our operations primarily through the aggregate net proceeds from equity financings (including from our IPO and pre-IPO sales of our convertible preferred stock) and borrowings under our loan and security agreement.

As of December 31, 2024 and December 31, 2023, we had cash and cash equivalents of $168.2 million and $82.5 million, respectively. On February 6, 2024, we issued 9,246,000 shares of common stock in our IPO, which included the exercise in full by the underwriters of their option to purchase 1,206,000 additional shares. The price to the public for each share was $16.00. The aggregate net proceeds from our IPO were $133.0 million, after underwriting discounts and commissions and other offering expenses of $4.6 million.

***Amended Loan and Security Agreement***

In December 2022, we entered into the Original Loan Agreement with the Lender, K2 HealthVentures LLC, as administrative agent for the Lender, and Ankura Trust Company, LLC, as collateral agent for the Lender. In January 2025, we entered into an amendment to the Original Loan Agreement (the Amendment, and the Original Loan Agreement as amended thereby, the Amended Loan Agreement) to, among other things, extend the Term Loan (as defined below) maturity date and increase the maximum available amount of term loans. The Amended Loan Agreement provides for up to an aggregate principal amount of $75.0 million in term loans, which we refer to collectively as the Term Loan, consisting of a first tranche term loan of $20.0 million, a second tranche term loan of up to an additional $30.0 million available at our request until December 15, 2025, subject to certain time-based, clinical milestones, and an additional third tranche term loan of up to an additional $25.0 million available at our request subject to the Lender's approval. We drew $20.0 million upon entry into the Amendment (approximately $10.0 million of which was used to refinance obligations under the Original Loan Agreement and pay fees and expenses incurred in connection with the Amendment).

As of December 31, 2024, we had an outstanding principal balance of $10.0 million under the Original Loan Agreement and, as of such date, based upon the terms of the Original Loan Agreement we could potentially access up to $10.0 million of the remaining $25.0 million available under the Original Loan Agreement. As of the date of the Amendment, and following the related refinancing, we had an outstanding principal balance of $20.0 million under the Term Loan.

The Term Loan matures on January 1, 2029. The Amended Loan Agreement provides for an interest only period until January 1, 2027, which may be extended to January 1, 2028, subject to the funding of at least $20.0 million of the second tranche term loan, following which the Terms Loan shall be repaid in equal monthly payments through the Term Loan maturity date.

Borrowings under the Amended Loan Agreement bear interest at (i) a variable per annum cash pay rate equal to the Prime Rate plus 1.45% (subject to a floor of 8.45% per annum) and (ii) a fixed per annum paid-in-kind rate equal to 1.0%. Interest is due and payable monthly in arrears. The Term Loan is secured by substantially all of our assets, excluding intellectual property. Upon final payment or prepayment of the Term Loan, we are required to pay a final payment equal to 5.95% of the amount borrowed.

We have the option to prepay all, but not less than all, of the Term Loan prior to the Term Loan maturity date, which would require that we pay the Lender a prepayment penalty fee based on a percentage of the outstanding principal balance, equal to 3% if the payment occurs on or before 24 months after the initial funding date, 2% if the prepayment occurs more than 24 months after, but on or before 36 months after the initial funding date, or 1% if the prepayment occurs more than 36 months after the initial funding date. No prepayment penalty fee is required if the Term Loan is prepaid within six months prior to the Term Loan maturity date or refinanced with the Lender. We were obligated to pay the Lender a one-time facility fee of $250,000 on the closing date of the Amendment. We are also obligated to pay a 0.5% fee multiplied by the third tranche term loan amount at the time of funding of the third trance term loan. Our obligation under the Original Loan Agreement to pay the Lender a one-time fee of $625,000 on the earlier of December 1, 2026 or earlier prepayment of the Term Loan remains outstanding.

Following an initial period with no financial covenants, beginning January 1, 2026, we must maintain a cash runway of at least five months, provided that this covenant will be waived during any period in which our market capitalization exceeds $700.0 million.

Additionally, under the terms of the Amended Loan Agreement, the Lender may, at its option, elect to convert up to $9.0 million of the then outstanding Term Loan ($4.0 million of which was reflected in the Original Loan Agreement and $5.0 million of which is reflected in the Amendment) into shares of our common stock.

***Convertible Grant Agreement***

In July 2024, we entered into the Convertible Grant Agreement with Wellcome. The Convertible Grant Agreement provides for an unsecured convertible loan, or the Convertible Loan, from Wellcome of up to approximately $11.7 million, payable in six tranches, $1.3 million of which was funded upon the execution of the Convertible Grant Agreement, and the remainder of which will be funded upon draw down of the remaining initiation payment or the completion of certain milestones as set forth in the Convertible Grant Agreement, subject to certain conditions described therein which may or may not be achieved. As of January 2025, we achieved a milestone under the Convertible Grant Agreement giving us the right to draw down a total of $3.8 million which represents the milestone and the remaining portion of the initiation payment.

We may use proceeds from the Convertible Loan solely to advance development of ALTO-100 in bipolar depression. In addition, if we do not exploit or develop ALTO-100 (other than for safety or efficacy concerns) within a specified period following the completion of our Phase 2b clinical trial evaluating ALTO-100 in patients with bipolar depression, the Convertible Grant Agreement provides Wellcome with a limited right to exploit ALTO-100, solely in bipolar depression, subject to a revenue share between Wellcome and us of any proceeds arising from Wellcome's exploitation. Outstanding amounts under the Convertible Loan accrue interest at an annual rate equal to the Sterling Overnight Index Rate plus 2%, subject to potential adjustment if such interest rate equals or exceeds 9% at any time. At any time after the second anniversary of the effective date of the Convertible Grant Agreement or in connection with an event of default, Wellcome has the right, at its election, to convert some or all of the Convertible Loan into shares of our common stock at a price per share equal to a 20% discount to the thirty-day volume-weighted average price of Common Stock on the New York Stock Exchange at the date of such conversion. The Convertible Grant Agreement provides that in no event shall the aggregate number of shares of our common stock issued pursuant to conversion of the Convertible Loan exceed 5,363,326, which is equal to 19.9% of the number of shares of our common stock outstanding as of the date of the Convertible Grant Agreement. At any time after the fifth anniversary of the date of the Convertible Grant Agreement or in connection with an event of default, Wellcome may require repayment of the Convertible Loan in full, together with accrued interest, to the extent not converted as described above.

***Shelf Registration Statement and Sales Agreement***

On February 3, 2025, we filed a shelf registration statement on Form S-3 with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof up to a total aggregate offering price of $300.0 million. We also simultaneously entered into a Sales Agreement, or the Sales Agreement, with Leerink Partners LLC, or the Sales Agent, pursuant to which we may issue and sell, from time to time at our discretion,

shares of our common stock having an aggregate offering price of up to $75.0 million through or to the Sales Agent. No shares of common stock have been issued and sold to date pursuant to the Sales Agreement.

***Cash Flows***

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

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Net cash used in operating activities | $ (47,424) | $ (33,448) |
| Net cash used in investing activities | (2,075) | (470) |
| Net cash provided by financing activities | 135,691 | 68,130 |
| Effect of exchange rate changes on cash, cash equivalents and restricted cash | (11) | (8) |
| Net increase in cash, cash equivalents and restricted cash | $ 86,181 | $ 34,204 |

*Operating activities*

Net cash used in operating activities was $47.4 million for the year ended December 31, 2024, as compared to $33.4 million for the year ended December 31, 2023. The increase in cash used was primarily the result of the increase in net loss of $25.1 million. The increase in net loss was offset by:

- increased non-cash expenses including stock-based compensation expenses which increased by $4.7 million to $7.6 million for the year ended December 31, 2024, compared to $2.9 million for the year ended December 31, 2023, and $0.7 million of non-cash expense in the year ended December 31, 2024 related to the achievement of a milestone related to a license agreement which was settled, in part, through the issuance of shares of our common stock.

- increased accrued expenses and other liabilities of $4.0 million in the year ended December 31, 2024 compared to a decrease in accrued expenses and other liabilities of $0.4 million in the year ended December 31, 2023.

*Investing activities*

Net cash used in investing activities was $2.1 million for the year ended December 31, 2024, as compared to $0.5 million for the year ended December 31, 2023 for corporate and clinical trial related capital expenditures, primarily related to the purchase of EEG machines utilized in our clinical trials.

*Financing activities*

Net cash provided by financing activities was $135.7 million for the year ended December 31, 2024, related to the issuance of 9,246,000 shares of common stock in our IPO at a price to the public of $16.00 per share, offset by $3.2 million of other offering expenses related to our IPO that were paid during the year ended December 31, 2024.

Net cash provided by financing activities was $68.1 million for the year ended December 31, 2023, related to the issuance of Series B convertible preferred stock of $25.0 million, and issuance of Series C preferred stock of $45.0 million, partially offset by share issuance costs of $0.7 million and payment of deferred offering costs of $1.4 million.

***Future Funding Requirements***

We believe that our existing cash and cash equivalents, together with the net proceeds from our IPO which was completed in February 2024, will be sufficient to fund our operating expenses and capital expenditure requirements into 2028. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could expend our capital resources sooner than we currently expect.

We will need substantial additional capital to develop our product candidates and fund operations for the foreseeable future. Our future capital requirements will depend on many factors, including:

- the scope, timing, rate of progress, and costs of our clinical trials for our current and any future product candidates;
- the number and scope of clinical programs we decide to pursue;
- the cost, timing, and outcome of preparing for and undergoing regulatory review of our current and any future product candidates;
- the cost and timing of manufacturing our product candidates;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending intellectual property-related claims;
- the terms and timing of establishing and maintaining collaborations, licenses, and other similar arrangements;
- the timing of any milestone and royalty payments to our existing or future suppliers, collaborators, or licensors;
- our efforts to enhance operational systems and our ability to attract, hire, and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;
- the extent to which we acquire or in-license other product candidates and technologies;
- the extent to which we enter into licensing or collaboration arrangements for any of our programs; and
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales, and distribution of our product candidates, if they receive marketing approval.

Until such time, if ever, as we can generate substantial revenue from product sales to support our cost structure, we expect to finance our cash needs through the public or private sale of equity, government or private party grants, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders may be diluted, and the terms of these securities may include liquidation or other preferences and anti-dilution protections that could 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, which could adversely impact our ability to conduct our business, and may require the issuance of warrants, which could potentially dilute the ownership interests of our stockholders. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates or may have to grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings on acceptable terms when needed, we may be required to delay, limit, reduce, or terminate our drug development or future commercialization efforts or grant rights to develop and market our current or any future product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

***Contractual Obligations and Commitments***

In addition to ongoing needs to fund our operations, our material cash requirements as of December 31, 2024 consist primarily of obligations under our Amended Loan Agreement, and lease commitment over the next five years. For additional information regarding our Loan Agreement and the Amended Loan Agreement, see “Item 8. Financial Statements - Note 8. Debt”. For additional information regarding our lease commitment, see “Item 8. Financial Statements - Note 7. Leases”.

We enter into contracts in the normal course of business with clinical trial sites and clinical supply manufacturers and with vendors for preclinical studies and clinical trials, research supplies, and other services and products for operating purposes. These contracts generally provide for termination after a notice period, and, therefore, we believe that our non-cancelable obligations under these agreements are not material.

In addition, we enter into agreements in the normal course of business with clinical trial sites, CROs, CMOs, and other vendors for research and development services. Such agreements generally provide for termination upon limited written notice. These payments are therefore not included in our contractual obligations discussion above. For additional information regarding our contractual obligations and commitments, see "Item 8. Financial Statements - Note 15. Commitments and Contingencies."

We are also party to certain collaboration and license agreements, which contain a number of contractual obligations. Those contractual obligations may entitle us to receive, or may obligate us to make, certain payments. The amount and timing of those payments are unknown or uncertain as we are unable to estimate the timing or likelihood of the events that will obligate those payments. We have milestones, royalties, and/or other payments due to third parties under our existing license agreements. See "Item 1. Business—License and Other Agreements" and "Item 8. Financial Statements – Note 10. Asset Purchase and License Agreements." We could not estimate when such payments will be due, and none of these events were probable to occur as of December 31, 2024.

**Critical Accounting Policies and Significant Judgments and Estimates**

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

We define our critical accounting policies as those accounting principles that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. While our significant accounting policies are more fully described in our audited consolidated financial statements (see "Item 8. Financial Statements – Note 3. Summary of Significant Accounting Policies"), we believe the following are the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments.

***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, including our site contracts for sites that are participating in our ongoing clinical studies, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

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

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period.

Costs incurred in obtaining technology licenses through asset acquisitions or in-licensing arrangements are charged to research and development expense if the acquired technology has not reached technological feasibility and has no alternative future use.

***Stock-Based Compensation***

We measure the cost of employee, nonemployee, and director services received in exchange for an award of equity instruments based on the fair value of the award on the date of grant and recognize the related expense over the period during which the employee, nonemployee or director is required to provide service in exchange for the award on a straight-line basis.

We estimate the fair value of each award on the date of grant using the Black-Scholes option-pricing model. This model requires the use of highly subjective assumptions to determine the fair value of each stock-based award, including:

- Fair value of common stock. See "—Determination of the Fair Value of Common Stock" below.
- Expected term. The expected term represents the period that the stock-based awards are expected to be outstanding. The expected term for our stock options was calculated based on the weighted-average vesting term of the awards and the contract period, or simplified method.
- Expected volatility. Since we do not have sufficient trading history to estimate the volatility of our common stock, the expected volatility was estimated based on the average historical volatility of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies 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 a treasury instrument whose term is consistent with the expected term of the stock options.
- 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.

Changes in the foregoing assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop. See Item 8. Financial Statements – Note 11. Stock Based Plans for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted in the periods presented.

As of December 31, 2024, there was $19.9 million of unrecognized stock-based compensation expense related to our granted service-based vesting options, which we expect to recognize over a remaining weighted-average period of 2.9 years.

***Determination of the Fair Value of Common Stock***

As there was no public market for our common stock prior to our IPO, the estimated fair value of our common stock underlying our stock-based awards historically has been determined by our board of directors as of each option grant date with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, or the Practice Aid. In valuing our common stock, the equity value of the business was determined using the backsolve method, a form of the subject company transaction method, wherein the equity value for a privately held company is derived from a recent transaction in our securities. The value was then allocated using the hybrid method allocation methodology. In accordance with Practice Aid, we used a hybrid method, which is a hybrid between the option pricing method, or OPM, and the probability-weighted expected return method, or PWERM. The hybrid method is a combination of the PWERM and OPM.

The OPM allocates the overall company value to the various share classes based on differences in liquidation preferences, participation rights, dividend policy, and conversion rights, using a series of call options. The call right is valued using a Black-Scholes option pricing model. The PWERM employs additional information not used in the OPM, including various market approach calculations depending upon the likelihood of various discrete future liquidity scenarios, such as an initial public offering or sale of the company, as well as the probability of remaining a private company. In a hybrid method, various exit scenarios are analyzed. A discount for lack of marketability of our common stock was then applied to arrive at an indication of value for the common stock.

In addition to considering the results of these third-party valuations, we considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, which may be a date later than the most recent third-party valuation date, including:

- the prices of our convertible preferred stock sold to or exchanged between outside investors in arm's length transactions, and the rights, preferences and privileges of our convertible preferred stock as compared to those of our common stock, including the liquidation preferences of our convertible preferred stock;
- the progress of our research and development efforts, including the status of preclinical studies and ongoing and planned 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;
- our financial position, including cash on hand, and our historical and forecasted performance and results of operations;
- the lack of an active public market for our common stock and our convertible preferred stock;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering, or a sale of our company, given prevailing market conditions;
- the achievement of enterprise milestones, including entering into collaboration and license agreements;
- the analysis of initial public offerings and the market performance of similar companies in the biotechnology industry; and
- the economy in general.

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 used significantly different estimates and assumptions, our stock-based compensation expense could be materially different. Following the IPO, the fair value of our common stock is determined based on the quoted market price of our common stock on the New York Stock Exchange.

**Emerging Growth Company and Smaller Reporting Company Status**

We are an "emerging growth company" as defined in the JOBS Act, and we may remain an emerging growth company for up to five years following the completion of our IPO. For so long as we remain an emerging growth company, we are permitted and intend to rely on certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved. In particular, in this Annual Report, we have provided only two years of audited financial statements and have not included all of the executive compensation-related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have elected to take advantage of the benefits of this extended transition period, and therefore, we are not subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies; however, we may adopt certain new or revised accounting standards early. We would cease to be an "emerging

growth company" upon the earliest to occur of: (i) the last day of the fiscal year in which we have $1.235 billion or more in annual revenue; (ii) the date on which we first qualify as a large accelerated filer under the rules of the SEC; (iii) the date on which we have, in any three-year period issued more than $1.0 billion in non-convertible debt securities; and (iv) the last day of the fiscal year ending after the fifth anniversary of our IPO (December 31, 2029).

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

**Off-Balance Sheet Arrangements**

In connection with our office lease, we have a standby letter of credit issued on our behalf with $0.5 million available and no amounts outstanding as of December 31, 2024. Since our inception, we have not had any relationships with unconsolidated organizations or financial partnerships, such as structured finance or special purpose entities that would have been established for the purpose of facilitating off-balance sheet arrangement.

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

As a "smaller reporting company" as defined by Item 10 of Regulation S-K, the Company is not required to provide the information required by this item.

**Item 8. Financial Statements and Supplementary Data.**


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|---|---|
| **Audited Consolidated Financial Statements as of and for the Years Ended December 31, 2024 and 2023:** | |
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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Alto Neuroscience, Inc.

### Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Alto Neuroscience, Inc. and subsidiary (the "Company") as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2024, and the related notes (collectively referred to as the "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 each of the two years in the period ended December 31, 2024, in conformity with accounting principles generally accepted in the United States of America.

### Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP

Chicago, Illinois
March 20, 2025

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

**Alto Neuroscience, Inc. and Subsidiary**
**Consolidated Balance Sheets**
(in thousands, except per share amounts)

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 168,229 | $ 82,548 |
| Prepaid expenses and other current assets | 1,108 | 2,843 |
| Total current assets | 169,337 | 85,391 |
| Restricted cash | 500 | — |
| Property and equipment, net | 2,666 | 1,106 |
| Operating right-of-use asset | 5,035 | — |
| Other assets | 4 | 131 |
| Total assets | $ 177,542 | $ 86,628 |
| **Liabilities, convertible preferred stock and stockholders' equity (deficit)** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,579 | $ 1,074 |
| Accrued expenses and other current liabilities | 8,429 | 4,536 |
| Total current liabilities | 10,008 | 5,610 |
| Term loan, non-current | 10,254 | 9,861 |
| Convertible Grant Agreement | 1,304 | — |
| Preferred stock warrant liability | — | 1,352 |
| Lease liability, long-term | 4,516 | — |
| Total liabilities | 26,082 | 16,823 |
| Commitments and contingencies (Note 15) | | |
| Convertible preferred stock | — | 141,477 |
| Stockholders' equity (deficit): | | |
| Common stock (par value $0.0001), 500,000 and 52,000 shares authorized; 26,987 and 3,832 shares issued and outstanding as of December 31, 2024 and 2023 | 3 | — |
| Additional paid-in capital | 289,954 | 5,372 |
| Accumulated deficit | (138,396) | (76,965) |
| Accumulated other comprehensive loss | (101) | (79) |
| Total stockholders' equity (deficit) | 151,460 | (71,672) |
| Total liabilities, convertible preferred stock and stockholders' equity (deficit) | $ 177,542 | $ 86,628 |

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

**Alto Neuroscience, Inc. and Subsidiary**
**Consolidated Statements of Operations and Comprehensive Loss**
(in thousands, except per share amounts)

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Operating expenses: | | |
| Research and development | $ 46,996 | $ 30,291 |
| General and administrative | 21,614 | 7,518 |
| Total operating expenses | 68,610 | 37,809 |
| Loss from operations | (68,610) | (37,809) |
| Other income (expense): | | |
| Interest income | 8,851 | 2,349 |
| Interest expense | (1,375) | (1,370) |
| Other, net | (297) | 525 |
| Total other income, net | 7,179 | 1,504 |
| Net loss | $ (61,431) | $ (36,305) |
| Other comprehensive loss: | | |
| Foreign currency translation | (22) | (33) |
| Total other comprehensive loss | (22) | (33) |
| Comprehensive loss | $ (61,453) | $ (36,338) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (2.50) | $ (9.73) |
| Weighted-average number of common shares outstanding, basic and diluted | 24,602 | 3,731 |

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

**Alto Neuroscience, Inc. and Subsidiary**
**Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)**
(in thousands)

| | Preferred Stock | | Common Stock | | Additional Paid-in Capital | Accumulated Deficit | Accumulated Other Comprehensive Loss | Total Stockholders Equity (Deficit) |
|---|---|---|---|---|---|---|---|---|
| | Shares (#) | Amount ($) | Shares (#) | Amount ($) | | | | |
| **Balance at December 31, 2022** | **16,204** | **$ 72,235** | **3,764** | **$ —** | **$ 2,300** | **$ (40,660)** | **$ (46)** | **$ (38,406)** |
| Exercise of common stock options | — | — | 68 | — | 181 | — | — | 181 |
| Issuance of Series B preferred stock, net of issuance costs of $154 | 4,167 | 24,846 | — | — | — | — | — | — |
| Issuance of Series C preferred stock, net of issuance costs of $604 | 9,548 | 44,396 | — | — | — | — | — | — |
| Foreign currency translation | — | — | — | — | — | — | (33) | (33) |
| Stock-based compensation expense | — | — | — | — | 2,891 | — | — | 2,891 |
| Net loss | — | — | — | — | — | (36,305) | — | (36,305) |
| **Balance at December 31, 2023** | **29,919** | **$ 141,477** | **3,832** | **$ —** | **$ 5,372** | **$ (76,965)** | **$ (79)** | **$ (71,672)** |
| Exercise of common stock options | — | — | 125 | — | 187 | — | — | 187 |
| Issuance of common stock for conversion of preferred stock | (29,919) | (141,477) | 13,664 | 2 | 141,475 | — | — | 141,477 |
| Exercise of warrant | — | — | 73 | — | — | — | — | — |
| Initial public offering of common stock, net of offering costs of $4,618 | — | — | 9,246 | 1 | 132,959 | — | — | 132,960 |
| Reclassification of warrant to equity | — | — | — | — | 1,595 | — | — | 1,595 |
| Issuance of common stock for MedRx Agreement | — | — | 47 | — | 735 | — | — | 735 |
| Foreign currency translation | — | — | — | — | — | — | (22) | (22) |
| Stock-based compensation expense | — | — | — | — | 7,631 | — | — | 7,631 |
| Net loss | — | — | — | — | — | (61,431) | — | (61,431) |
| **Balance at December 31, 2024** | **—** | **$ —** | **26,987** | **$ 3** | **$ 289,954** | **$ (138,396)** | **$ (101)** | **$ 151,460** |

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

**Alto Neuroscience, Inc. and Subsidiary**
**Consolidated Statements of Cash Flows**
(in thousands)

| | Year Ended December 31, 2024 | 2023 |
|---|---|---|
| **Cash Flows from Operating Activities:** | | |
| Net loss | $ (61,431) | $ (36,305) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Stock-based compensation expense | 7,631 | 2,891 |
| Depreciation and amortization | 502 | 373 |
| Non-cash research and development license expense | 735 | — |
| Non-cash lease expense | 337 | 280 |
| Non-cash interest expense related to term loan | 393 | 396 |
| Loss on disposal of assets | 52 | 140 |
| Change in other, net | 297 | (525) |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other assets | (463) | 291 |
| Accounts payable | 516 | (632) |
| Accrued liabilities and other liabilities | 4,007 | (357) |
| Net cash used in operating activities | (47,424) | (33,448) |
| **Cash Flows from Investing Activities:** | | |
| Capital expenditures | (2,075) | (470) |
| Net cash used in investing activities | (2,075) | (470) |
| **Cash Flows from Financing Activities:** | | |
| Proceeds from issuance of common stock from initial public offering | 137,579 | — |
| Payments of initial public offering costs | (3,225) | (1,393) |
| Issuance of convertible preferred stock | — | 70,000 |
| Payments on issuance cost from Series B and Series C preferred stock financings | (100) | (658) |
| Proceeds from Convertible Grant Agreement | 1,250 | — |
| Proceeds from exercise of stock options | 187 | 181 |
| Net cash provided by financing activities | 135,691 | 68,130 |
| Effect of exchange rate changes on cash, cash equivalents and restricted cash | (11) | (8) |
| Net increase in cash, cash equivalents and restricted cash | 86,181 | 34,204 |
| Cash, cash equivalents and restricted cash at the beginning of the period | 82,548 | 48,344 |
| Cash, cash equivalents and restricted cash at the end of the period | $ 168,729 | $ 82,548 |
| **Supplemental Disclosure of Non-cash Activities** | | |
| Deferred offering and share issue costs not yet paid | $ 8 | $ 916 |
| Conversion of preferred stock into common stock upon completion of initial public offering | $ 141,477 | $ — |
| Reclassification of preferred warrant liability to equity | $ 1,595 | $ — |
| Reclassification of deferred offering costs to equity | $ 1,393 | $ — |
| Operating right-of-use asset obtained in exchange for lease obligation | $ 5,246 | $ — |
| **Supplemental Disclosure of Cash Flow Information** | | |
| Cash paid for interest | $ 999 | $ 912 |

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

## 1. Description of the Business

Alto Neuroscience, Inc. (the "Company" or "Alto") was incorporated in Delaware on March 25, 2019. The Company maintains its headquarters in Mountain View, California. The Company has one wholly-owned subsidiary in Australia that was formed during 2020 to conduct clinical trials.

Alto is a clinical stage biopharmaceutical company with a mission to redefine psychiatry by leveraging individuals' neurobiology to develop personalized and highly effective treatment options. Through insights derived from the Company's scalable and proprietary Precision Psychiatry Platform, the Company aims to discover brain-based biomarkers to better identify which patients are more likely to respond to its novel product candidates. The Company's current pipeline consists of five clinical-stage assets addressing high-need therapeutic areas, including major depressive disorder ("MDD"), bipolar depression ("BPD"), and schizophrenia, as identified by independent brain-based biomarkers.

### Liquidity and Capital Resources

The Company has incurred significant operating losses since inception and has relied upon equity financings to fund its operations. At December 31, 2024, the Company had an accumulated deficit of $138.4 million. As the Company continues to incur losses, its transition to profitability will depend on the successful development, approval and commercialization of product candidates and on the generation of sufficient revenues to support its cost structure. No assurance can be provided that the Company will ever be profitable, and unless or until it becomes profitable, the Company will need to continue to raise additional capital.

In February 2024, the Company completed its initial public offering ("IPO") of its common stock. The Company issued and sold 9,246,000 shares of common stock at a public offering price of $16.00 per share, which included 1,206,000 shares sold pursuant to the exercise of the underwriters' option to purchase additional shares, and received net proceeds of $133.0 million after deducting underwriting discounts and commissions and other offering costs. Upon completion of the IPO, all outstanding shares of the Company's outstanding preferred stock converted into an aggregate of 13,664,261 shares of common stock. In addition, the IPO resulted in the net exercise and conversion of all outstanding Series A Preferred Stock Warrants for an aggregate of 72,631 shares of common stock. During the year ended December 31, 2023, the Company sold and issued 4,166,667 shares of Series B convertible preferred stock for gross proceeds of $25.0 million and sold and issued 9,547,802 shares of Series C convertible preferred stock for gross proceeds of $45.0 million.

Management believes that its existing financial resources are sufficient to continue operating activities at least one year past the issuance date of these consolidated financial statements. The Company has based this estimate on assumptions that may prove to be wrong, and its operating plan may change as a result of many currently unknown factors. As a result, the Company could deplete its capital resources sooner than it currently expects. Future capital requirements will depend on many factors, including the timing and extent of spending on research and development and the market acceptance of the Company's products. The Company will need to obtain additional financing in order to complete clinical studies and launch and commercialize any product candidates for which it receives regulatory approval. There can be no assurance that such financing will be available on acceptable terms or at all. However, the Company expects to finance its future cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, or licensing arrangements. If the Company is unable to obtain funding, the Company would be forced to delay, reduce, or eliminate some or all of its research and development programs, preclinical and clinical testing or commercialization efforts, which could adversely affect its business prospects.

## 2. Basis of Presentation

The accompanying consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") as determined by the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

The accompanying consolidated financial statements include the accounts of Alto and its wholly-owned subsidiary. All intercompany transactions and balances have been eliminated in consolidation.

**Emerging Growth Company Status and Smaller Reporting Company Status**

The Company is an emerging growth company ("EGC"), as defined in the Jumpstart Our Business Startups Act (the "JOBS Act"), enacted in 2012. Under the JOBS Act, EGCs can delay adopting new or revised accounting standards issued after the enactment of the JOBS Act until those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an EGC or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

The Company is also a "smaller reporting company" as defined in the Exchange Act. The Company may continue to be a smaller reporting company even after the Company is no longer an EGC. The Company may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as its voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of its second fiscal quarter, or its annual revenue is less than $100.0 million during the most recently completed fiscal year and its voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of its second fiscal quarter.

**Stock Splits**

In January 2023, the Company's Board of Directors (the "Board") approved a 1.1156 for 1 forward stock split of the Company's issued and outstanding shares of Series B Preferred Stock, and a proportional adjustment to the existing conversion ratio, as well as the exercise price of the then-outstanding K2 Warrant. Accordingly, all Series B share and per share amounts for all periods presented in the financial statements have been adjusted retroactively, where applicable, to reflect this stock split and adjustment of the preferred stock conversion ratio.

In January 2024, the Board approved a 1 for 2.2241 reverse stock split of the Company's issued and outstanding shares of common stock and options to purchase common stock under its 2019 Equity Incentive Plan. The reverse stock split reduced the number of shares of the Company's issued and outstanding common stock, as well as the numbers of shares reserved and available for future issuance and underlying outstanding options to purchase common stock under its 2019 Equity Incentive Plan, on a 1 for 2.2241 basis, and resulted in an adjustment to the respective conversion ratios for the Company's Series Seed convertible preferred stock, Series A convertible preferred stock, Series B convertible preferred stock, and Series C convertible preferred stock to account for the reverse stock split on any conversion of such series of convertible preferred stock into common stock. The reverse stock split did not affect the par values per share, and has been adjusted retroactively in the financial statements, where applicable.

**Recently Adopted Accounting Pronouncements**

In June 2016, the FASB issued Accounting Standards Update ("ASU") No. 2016-13, *Financial Instruments — Credit Losses: Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). The guidance is effective for the Company beginning January 1, 2023 and changes how entities account for credit losses on financial assets and other instruments that are not measured at fair value through net income, including available-for-sale debt securities. The Company adopted the provisions of ASU 2016-13 prospectively beginning January 1, 2023. The adoption did not have a material impact on the Company's consolidated financial statements.

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting - Improving Reportable Segment Disclosures (Topic 280)*. The standard requires disclosures to include significant segment expenses that are regularly provided to the chief operating decision maker ("CODM"), a description of other segment items by reportable segment, and any additional measures of a segment's profit or loss used by the CODM when deciding how to allocate resources. The ASU also requires all annual disclosures currently required by Topic 280 to be included in interim periods. The Company adopted this ASU as of December 31, 2024 with retrospective application to all periods presented in these financial statements. Refer to Note 17 for additional information.

**Accounting Pronouncements Not Yet Adopted**

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740) : Improvements to Income Tax Disclosures*. The standard expands the disclosure requirements for income taxes, specifically related to the rate reconciliation and income taxes paid. The standard will be effective starting in annual periods beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact the adoption of this standard will have on its consolidated financial statement disclosures.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement – Reporting Comprehensive Income – Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, which expands disclosures about specific expense categories presented on the face of the income statement. The standard is effective for annual reporting periods beginning after December 15, 2026 and interim reporting periods beginning after December 15, 2027. The Company is currently evaluating the impact the adoption of this standard will have on its consolidated financial statements.

In November 2024, the FASB issued ASU No. 2024-04, Debt – *Debt with Conversion and Other Options (Subtopic 470-20): Induced Conversions of Convertible Debt Instruments*, which affects entities that settle convertible debt instruments for which the conversion privileges were changed to induce conversion. The standard is effective for annual reporting periods beginning after December 15, 2025, and interim reporting periods within those annual reporting periods. The Company is currently evaluating the impact the adoption of this standard will have on its consolidated financial statements.

## 3. Summary of Significant Accounting Policies

**Use of Estimates**

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results may differ materially from those estimates. The most significant estimates and assumptions in the Company's consolidated financial statements relate to the determination of the fair value of its common stock prior to the completion of the IPO (as an input for calculating stock-based compensation), estimating accrued or prepaid research and development expenses, and the valuation of the preferred stock warrant liability. These estimates and assumptions are based on current facts, historical experience, and various other factors 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 and the recording of expenses that are not readily apparent from other sources. To the extent there are material differences between the estimates and actual results, the Company's future results of operations will be affected.

**Cash and Cash Equivalents**

Cash and cash equivalents consist of cash and, if applicable, highly liquid investments with an original maturity of three months or less when purchased. As of December 31, 2024 and 2023, the Company held $168.2 million and $82.5 million in total cash and cash equivalents, respectively.

**Credit Risk**

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash and cash equivalents. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. Management believes that the Company is not exposed to significant credit risk as the Company's deposits are held at financial institutions that management believes to be of high credit quality. The Company has not experienced any losses on these deposits.

**Risk and Uncertainties**

The Company's future results of operations involve a number of risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, uncertainty of future clinical study results, the scope, rate of progress, and expense of the Company's ongoing as well as any additional non-clinical studies, clinical trials and other research and development activities, clinical trial

enrollment rate or design, the manufacturing of the Company's product candidates, significant and changing government regulation, and the timing and receipt of any regulatory approvals.

The Company's product candidates require approvals from the U.S. Food and Drug Administration and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any product candidates will receive the necessary approvals. If the Company was denied approval, approval was delayed, or the Company was unable to maintain approval for any product candidate, it could have a materially adverse impact on the Company.

The Company is dependent upon third-party manufacturers to supply product for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

**Fair Value of Financial Instruments**

ASC 820, *Fair Value Measurement* ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.
- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. See Note 8 and Note 14 for more information related to the Company's Level 3 fair value measurements.

The carrying values reported in the Company's balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable, and accrued expenses are reasonable estimates of their fair values due to the short-term nature of these items.

**Property and Equipment**

Property and equipment are stated at cost. Maintenance and repairs are charged to expense as incurred. Additions, major improvements, and replacements are capitalized. Depreciation of property and equipment is provided for by the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are capitalized and amortized over the shorter of the estimated useful lives of the assets or the remaining lease term. The estimated useful lives of other categories of property and equipment are as follows:

| Category: | Estimated Useful Life: |
|---|---|
| Computer software and equipment | 5 years |
| Leasehold improvements | 5 years |
| Office equipment and furniture | 7 years |
| Laboratory equipment | 5 years |

**Impairment of Long-Lived Assets**

Long-lived assets consist of property and equipment as well as right-of-use assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If the sum of the estimated future undiscounted cash flows expected to result from the use and eventual disposition of an asset is less than the carrying amount of the asset, an impairment loss is recognized. Measurement of an impairment loss is based on the fair value of the asset. The Company has not recorded any impairment losses on long-lived assets during the years ended December 31, 2024 and 2023.

**Leases**

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew. Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including a lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets.

**Debt Discount and Debt Issuance Costs**

Debt issuance costs are deferred and presented as a reduction to long-term debt. The initial fair value of the preferred stock warrant liability that was issued to the lender under the Company's loan agreement is treated as a debt discount. Debt discount and debt issuance costs are amortized using the effective interest rate method over the term of the loan.

Amortization of debt discount and debt issuance costs are included within interest expense in the consolidated statements of operations and comprehensive loss.

**Research and Development**

Research and development expenses are comprised of costs incurred in clinical trials and in research and development activities. Such costs include: contract services performed by third parties in accordance with agreements established with clinical research organizations ("CROs") and clinical trial sites; research agreements; laboratory costs and other supplies; and salaries and benefits, stock-based compensation, overhead costs, depreciation, and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

The Company has entered into various research and development contracts with research institutions, CROs, clinical manufacturing organizations, and other companies. These agreements are generally cancellable, and related payments are recorded as research and development expenses as incurred. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheet as prepaid or accrued expenses. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the prepaid or accrued expenses, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the accrued or prepaid balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Costs incurred in obtaining product rights or technology licenses through asset acquisitions or pursuant to licensing agreements are charged to research and development expense if the purchased or licensed technology has not reached technological feasibility and has no alternative future use.

**General and Administrative**

General and administrative expenses generally consist of costs related to personnel, including stock-based compensation, third party service providers and professional fees, general office expenses, an allocation of rent and utilities expense, and legal costs associated with patents.

**Stock-Based Compensation**

The Company has stock-based compensation plans that cover the Company's employees and nonemployees, which provide for grants of stock options, restricted stock awards ("RSAs"), and restricted stock units ("RSUs"). The Company expenses stock-based compensation related to stock options, RSAs and RSUs over the requisite service period using the straight-line method. All stock-based compensation costs are recorded in research and development expense or general and administrative expense in the consolidated statements of operations and comprehensive loss based upon the respective employee's role within the Company. Forfeitures are recorded as they occur.

**Deferred Initial Public Offering Costs**

Costs directly attributable to the Company's offering of its equity securities are deferred and capitalized as deferred offering costs. These costs primarily represent legal, underwriting and accounting costs related to the Company's efforts to raise capital through a public sale of its common stock. These costs were deferred until the completion of the IPO, which occurred on February 6, 2024, at which time such costs were reclassified to additional paid-in capital as a reduction of the IPO proceeds. At December 31, 2023, the Company had capitalized $2.2 million of deferred IPO costs, which are recorded within prepaid expenses and other current assets, respectively. At December 31, 2024, the Company had no capitalized deferred initial public offering costs.

**Convertible Preferred Stock**

The Company has applied the guidance in ASC 480-10-S99-3A, *SEC Staff Announcement: Classification and Measurement of Redeemable Securities* and has therefore classified its Series Seed, Series A, Series B and Series C convertible preferred stock as mezzanine equity. The convertible preferred stock was recorded outside of stockholders' equity (deficit) because, in the event of certain deemed liquidation events considered not solely within the Company's

control, such as a merger, acquisition or sale of all or substantially all of the Company's assets, the convertible preferred stock would become redeemable at the option of the holders. In the event of a deemed liquidation event, proceeds received from such transaction would have been distributed in accordance with the liquidation preferences set forth in the Company's amended and restated certificate of incorporation. The Company determined not to adjust the carrying values of the convertible preferred stock to the liquidation preferences of such shares because of the uncertainty of whether or when such an event would occur. All shares of the Company's previously issued and outstanding convertible preferred stock were converted into shares of common stock upon the closing of the IPO (see Note 14).

**Warrants**

The Company accounted for its freestanding warrants on its convertible preferred stock as liabilities at fair value, as the instruments underlying the warrants were classified outside of permanent equity. The preferred stock warrants were remeasured at each reporting period with changes in fair value recognized in the consolidated statements of operations and comprehensive loss. The preferred stock warrants continued to be remeasured to fair value until the earlier of the exercise of the preferred stock warrants, the expiration of the preferred stock warrants, or until such time as the preferred stock warrants are no longer considered liability instruments. All preferred stock warrants previously issued and outstanding were either exercised into shares of common stock or converted into common stock warrants upon the closing of the IPO (see Note 14), and are no longer subject to remeasurement.

**Net Loss Per Share**

Basic net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period excluding unvested restricted stock subject to repurchase. Diluted net loss per share is computed using the sum of the weighted-average number of shares of common stock outstanding during the period and the effect of dilutive securities.

The Company's convertible preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such participating securities.

**Comprehensive Loss**

Comprehensive loss comprises net loss and other comprehensive income or loss. Other comprehensive income or loss consists only of foreign currency translation adjustments related to the consolidation of the Company's foreign subsidiary.

**Foreign Currency**

Alto's functional currency is the U.S. dollar. The functional currency of the Company's foreign subsidiary is the same as its corresponding local currency. Assets and liabilities of the foreign subsidiary are translated at the spot rate in effect at the applicable reporting date. Likewise, expenses are translated at the average exchange rates in effect during the applicable period. The resulting foreign currency translation adjustment is recorded as accumulated other comprehensive income (loss), which is reflected as a separate component of stockholders' deficit. Foreign currency transaction gains and losses were not significant in any period presented.

**Income Taxes**

The Company accounts for income taxes under the liability method in accordance with FASB ASC 740, *Income Taxes*. Under this method, deferred income tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is established if it is more likely than not that all, or some portion, of deferred income tax assets will not be realized. The Company has recorded a full valuation allowance to reduce its net deferred income tax assets to zero. In the event the Company were to determine that it would be able to realize some or all its deferred income tax assets in the future, an adjustment to the deferred income tax asset valuation allowance would increase income in the period such determination was made.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained upon an examination. Any recognized income tax positions would be measured at the largest amount that is

greater than 50% likely of being realized. Changes in recognition or measurement would be reflected in the period in which the change in judgment occurs. At December 31, 2024 and 2023, the Company had no liability for income tax associated with uncertain tax positions. The Company would recognize any corresponding interest and penalties associated with its income tax positions in income tax expense. No income tax interest or penalties were incurred in the years ended December 31, 2024 and 2023.

### 4. Prepaid Expenses and Other Current Assets

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

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| Other prepaid expenses | $ 902 | $ 522 |
| Other current assets | 30 | 112 |
| Deferred offering costs | — | 2,209 |
| Prepaid insurance | 176 | — |
| Total prepaid expenses and other current assets | $ 1,108 | $ 2,843 |

### 5. Property and Equipment, Net

Property and equipment, net are as follows (in thousands):

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| Office equipment and furniture | $ 448 | $ 70 |
| Computer software and equipment | 670 | 519 |
| Laboratory equipment | 2,306 | 1,201 |
| Leasehold improvements | 246 | — |
| Less: accumulated depreciation | (1,004) | (684) |
| Property and equipment, net | $ 2,666 | $ 1,106 |

Depreciation and amortization expense was approximately $0.5 million and $0.4 million for the years ended December 31, 2024 and 2023, respectively.

### 6. Accrued Expenses and Other Current Liabilities

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

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| Accrued payroll, vacation and employee-related expenses | $ 4,951 | $ 518 |
| Accrued research | 1,625 | 2,328 |
| Accrued offering and share issue costs | — | 916 |
| Accrued license fees | — | 50 |
| Accrued interest, short term | 78 | 84 |
| Other accruals and current liabilities | 905 | 515 |
| Lease liability, short term | 870 | 125 |
| Total accrued expenses and other current liabilities | $ 8,429 | $ 4,536 |

## 7. Leases

On May 29, 2024, the Company and Mountain View City Center, LP ("Landlord") entered into a lease agreement (the "2024 Lease Agreement") for 16,332 square feet of office space in a multi-tenant building located in Mountain View, California with an initial lease term of 65 months. Including payments already made, the Company will make payments of approximately $7.1 million over the course of the initial term of the lease. In connection with the 2024 Lease Agreement, the Company secured a letter of credit amounting to $0.5 million, which was recorded in restricted cash on its consolidated balance sheet as of December 31, 2024. At the Company's option, it may renew the lease for one three-year period. The Company also has a one-time option to terminate the lease after the third lease year. If the Company elects to terminate the lease after the third lease year, including payments already made, the Company will make payments of approximately $4.0 million over the term of the lease.

The Company obtained control of the space in September 2024, and, accordingly, the Company recorded the liability associated with the 2024 Lease Agreement at the present value of the lease payments not yet paid, using the discount rate as of the commencement date. As the discount rate implicit in the 2024 Lease Agreement was not readily determinable, the Company utilized its incremental borrowing rate. The renewal or early termination options were not assumed to be exercised in the determination of the lease term, since they are not deemed to be reasonably certain at the inception of the lease. At lease commencement, the Company recorded an operating right-of-use asset and lease liability of $5.2 million.

The 2024 Lease Agreement does not contain material residual value guarantees, restrictions, or covenants.

The components of lease expense were as follows for the years ended December 31, 2024 and 2023 (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Operating lease expense | $ 551 | $ 295 |
| Variable lease expense | 53 | 28 |
| Total lease expense | $ 604 | $ 323 |

Short-term lease costs were not material for the years ended December 31, 2024 and 2023.

Supplemental cash flow information related to operating leases for the years ended December 31, 2024 and 2023 (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Cash paid for amounts included in the measurement of lease liabilities | $ 76 | $ 294 |

In addition to the above, during the year ended December 31, 2024, the Company made $0.1 million of payments related to its lease agreement for the office space in Los Altos, California, which concluded in the second quarter of 2024.

Supplemental balance sheet information related to operating leases as of December 31, 2024 and 2023 was as follows (in thousands):

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| Operating lease right-of-use assets | $ 5,035 | $ 125 |
| Operating lease liability—current portion (included in accrued expenses and other current liabilities) | 870 | 125 |
| Operating lease liability—long-term | 4,516 | — |
| Total operating lease liabilities | $ 5,386 | $ 125 |
| Weighted average remaining lease term (in years) | 5.3 | 0.5 |
| Weighted average discount rate | 9.71% | 4.45% |

As of December 31, 2024, the future payments under operating leases were as follows (in thousands):

| | |
|---|---|
| 2025 | $ 917 |
| 2026 | 1,216 |
| 2027 | 1,456 |
| 2028 | 1,500 |
| 2029 | 1,545 |
| Thereafter | 432 |
| Total lease payments | 7,066 |
| Less: imputed interest | (1,680) |
| Present value of lease payments | $ 5,386 |

**8. Debt**

On December 16, 2022, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with K2 HealthVentures LLC as a lender, and other lenders (collectively, "Lender"), K2 HealthVentures LLC, as administrative agent for Lender ("Administrative Agent"), and Ankura Trust Company, LLC, as collateral agent for Lender. The Lender has agreed to make available to the Company term loans in an aggregate principal amount of up to $35.0 million under the Loan Agreement. The Company plans to use the proceeds of the term loans to support clinical development as well as for working capital and general corporate purposes. The Loan Agreement provides a term loan commitment of $35.0 million in four potential tranches: (i) a $10.0 million term loan facility funded on December 16, 2022 (the "First Tranche Term Loan"), (ii) a $7.5 million term loan facility (the "Second Tranche Term Loan") available at the Company's request between October 1, 2023 and March 1, 2024, subject to either positive data from the Company's Phase 2b randomized controlled study of ALTO-100 or positive data from the Company's Phase 2b randomized controlled study of ALTO-300, in each case as determined by the Administrative Agent in its sole discretion, (iii) a $7.5 million term loan facility (the "Third Tranche Term Loan") available at the Company's request between October 1, 2023 and March 1, 2024, subject to positive data from the Company's Phase 2b randomized controlled study of ALTO-100 and positive data from the Company's Phase 2b randomized controlled study of ALTO-300, in each case as determined by the Administrative Agent in its sole discretion, and (iv) a $10.0 million term loan facility (the "Fourth Tranche Term Loan") available through January 1, 2025 at both the Lender's and the Company's option, subject to the Lender's review of the Company's financial and clinical information and operating plans and approval of the Lender's investment committee. All four of these term loans have a maturity date of December 1, 2026. Based upon the terms of the Loan Agreement the Company could potentially access up to $10.0 million of the remaining $25.0 million of the credit facility.

Borrowings under all four term loan facilities bear interest at a variable annual rate equal to the greater of (i) 6.70% and (ii) the Prime Rate plus 1.20%. The Company is permitted to make interest-only payments on the First Tranche Term Loan for the first 24 months following the funding date. The interest-only period can be extended by an additional 12 months, subject to the funding of the Second Tranche Term Loan or the funding of the Third Tranche Term Loan and if the Company has completed equity sales of greater than $75.0 million prior to January 1, 2025, subject to certain conditions. In addition, each term loan funded also accrues a deferred interest amount equal to 1% annually of the outstanding principal,

and becomes payable at the end of the 48-month term, or earlier in the instance of a repayment. The term of the combined facility will be 48 months, with repayment in monthly installments commencing at the end of the resulting interest-only period as outlined above through the end of the 48-month term.

The Company is obligated to pay a final fee equal to 6.25% of the aggregate amount of the term loans funded ("Exit Fee") to occur upon the earliest of (i) the maturity date, (ii) the acceleration of the term loans, and (iii) the prepayment of the term loans. The Company has the option to prepay all, but not less than all, of the outstanding principal balance of the term loans under the Loan Agreement. If the Company prepays all of the term loans prior to the maturity date, it will pay the Lender a prepayment penalty fee based on a percentage of the outstanding principal balance, equal to 3% if the payment occurs on or before 24 months after the initial funding date, 2% if the prepayment occurs more than 24 months after, but on or before 36 months after the initial funding date, or 1% if the prepayment occurs more than 36 months after the initial funding date. The Company was also obligated to pay the Lender a one-time facility fee of $0.2 million ("Facility Fee") on the initial closing date and will be obligated to pay a 0.7% fee on the amount of the Fourth Tranche Term Loan, if and when funded. The Exit Fee of $0.6 million and the Facility Fee of $0.2 million with respect to the First Tranche Term Loan were recorded as debt discount, and are being accreted using the effective interest method over the term of the First Tranche Term Loan within interest expense in the consolidated statements of operations and comprehensive loss.

The Lender may, at its option, elect to convert any portion of no more than $4.0 million of the then outstanding term loan amount and all accrued and unpaid interest thereon into shares of the Company's common stock at the Lender's election, at a conversion price of the lesser of $17.86 per share and the price per share of the next round of stock in the Company's next equity offering in which the Company receives at least $20.0 million of gross proceeds. The Company determined that the embedded conversion option is not required to be separated from the term loan as it qualifies for the derivative accounting scope exception since the preferred stock is not readily convertible to cash. In February 2024 the Company completed its IPO and the conversion option applies to the Company's common stock (see Note 1) at a conversion price of $10.49 per share. No amount has been converted into shares of common stock as of December 31, 2024.

The Company's obligations under the Loan Agreement are secured by a first priority security interest in substantially all of its assets (with an exclusion for intellectual property). The Loan Agreement contains customary representations and warranties, and also includes customary events of default, including payment default, breach of covenants, change of control, and material adverse effects. The Loan Agreement restricts certain activities, such as disposing of the Company's business or certain assets, incurring additional debt or liens or making payments on other debt, making certain investments and declaring dividends, acquiring or merging with another entity, engaging in transactions with affiliates or encumbering intellectual property, among others. There are no financial covenants associated with the Loan Agreement.

Upon the occurrence of an event of default, a default interest rate of an additional 5% per annum may be applied to the outstanding loan balances, and the Lender may declare all outstanding obligations immediately due and payable and exercise all of its rights and remedies as set forth in the Loan Agreement and under applicable law.

The Company recorded interest expense related to the Loan Agreement of $1.4 million for both the years ended December 31, 2024 and 2023, at a weighted-average rate of 10.5% and 10.4%, respectively.

Future principal debt payments and Exit Fee of the term loans funded as of December 31, 2024 are as follows (in thousands):

| | |
|---|---|
| 2025 | $ 4,767 |
| 2026 | 5,233 |
| 2027 | — |
| 2028 | — |
| Total principal payments | 10,000 |
| Exit Fee | 625 |
| Deferred interest | 210 |
| Total principal payments and Exit Fee | 10,835 |
| Less: Unamortized Exit Fee | (313) |
| Less: Unamortized debt discount related to warrants | (105) |
| Less: Unamortized debt issuance costs, including Facility Fee | (163) |
| Term loan, non-current | $ 10,254 |
| Less: Term loan, current portion | — |
| Term loan, non-current | $ 10,254 |

On January 13, 2025, the Company amended the Loan Agreement. See Note 18 for additional information. Since the principal amounts due within one year from the balance sheet have been refinanced on a long-term basis after the balance sheet date but before the issuance of these financial statements, the entire amount funded under the Loan Agreement has been classified as non-current as of December 31, 2024.

***The Wellcome Trust Limited Convertible Grant Agreement***

In July 2024, the Company entered into a convertible loan agreement (the "Convertible Grant Agreement") with The Wellcome Trust Limited ("Wellcome"). The Convertible Grant Agreement provides for an unsecured convertible loan (the "Convertible Loan") from Wellcome of up to approximately $11.7 million, payable to Alto in six tranches, of which up to $2.0 million could be funded upon the execution of the Convertible Grant Agreement and the remainder of which will be funded upon the completion of certain milestones as set forth in the Convertible Grant Agreement. As of December 31, 2024, the Company has drawn down $1.3 million of the $2.0 million execution tranche and will continue to access the loan as needed as the ALTO-100 study in bipolar depression progresses. Interest will accrue at an annual rate equal to the Sterling Overnight Index Rate plus 2%, subject to potential adjustment if such annual interest rate equals or exceeds 9% at any time. Proceeds from the Convertible Loan may be used by the Company solely to advance development of ALTO-100 in bipolar depression. The Convertible Grant Agreement also includes customary covenants, representations and warranties, including with respect to the conduct of the Company's Phase 2b clinical trial evaluating ALTO-100 in patients with bipolar depression and certain information and audit rights of Wellcome in connection therewith, as well as with respect to the Company's efforts to develop and exploit ALTO-100.

At any time after the second anniversary of the effective date of the Convertible Grant Agreement or in connection with an event of default, Wellcome has the right, at its election, to convert some or all of the Convertible Loan into shares of the Company's common stock at a price per share equal to a 20% discount to the thirty-day volume-weighted average price of Common Stock on the New York Stock Exchange at the date of such conversion. The Convertible Grant Agreement provides that in no event shall the aggregate number of shares of Common Stock issued pursuant to conversion of the Convertible Loan exceed 5,363,326, which is equal to 19.9% of the number of shares of Common Stock outstanding as of the date of the Convertible Grant Agreement. At any time after the fifth anniversary of the effective date of the Convertible Grant Agreement or in connection with an event of default, Wellcome may require repayment of the Convertible Loan in full, together with accrued interest, to the extent not converted as described above.

Future principal debt payments of the Convertible Grant Agreement funded as of December 31, 2024 are as follows (in thousands):

| | | |
|---|---|---|
| 2025 | $ | — |
| 2026 | | — |
| 2027 | | — |
| 2028 | | — |
| 2029 | | 1,250 |
| Term loan, non-current | $ | 1,250 |

The Company assessed the terms and features of the Convertible Grant Agreement and determined that the Company was eligible to elect the fair value option under ASC 825, *Financial Instruments*. The Convertible Grant Agreement contains various embedded features and the election of the fair value option allowed the Company to bypass analysis of potential embedded derivatives and further analysis of bifurcation of any recognized financial liabilities. Under the fair value option, the financial liability is initially measured at its fair value on the issue date and subsequently remeasured at estimated fair value on a recurring basis at each reporting date. Changes in the fair value of the Convertible Grant Agreement, which include accrued interest, if any, are recorded as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. The Company has not elected to present interest expense separately from changes in fair value and therefore will not present interest expense associated with the Convertible Grant Agreement. Any changes in fair value caused by instrument-specific credit risk are presented separately in other comprehensive income or loss.

The Company determined the fair value of the Convertible Grant Agreement using a probability-weighted income approach and recorded the loan at fair value of $1.3 million in the consolidated balance sheet at issuance. The Company calculated the discounted cash flows of the Convertible Grant Agreement using a discount rate of 11.17% and adjusted for the probability of repayment and conversion scenarios. The Company remeasured the fair value of the Convertible Grant Agreement as of December 31, 2024 using a probability-weighted income approach. The Company calculated discounted cash flows of the Convertible Grant Agreement using a discount rate of 11.57% and adjusted for the probability of various repayment scenarios.

The following table reconciles the change in fair value of the Convertible Grant Agreement during the year ended December 31, 2024 (in thousands):

| | | |
|---|---|---|
| Beginning fair value balance, July 2024 | $ | — |
| Recognition of Convertible Grant Agreement | | 1,250 |
| Principal payments | | — |
| Changes in fair value reported in statement of operation | | 54 |
| Changes in fair value reported in comprehensive loss | | — |
| Ending fair value balances as of December 31, 2024 | $ | 1,304 |

**9. Fair Value**

The Company's financial instruments that are measured at fair value on a recurring basis consist of money market funds and the Convertible Grant Agreement. The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy used to determine such fair values (in thousands):

| | December 31, 2024 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| Assets: | | | | |
| Cash and cash equivalents: | | | | |
| Money market funds | $ 168,136 | $ 168,136 | $ — | $ — |
| Restricted cash: | | | | |
| Money market funds | 500 | 500 | — | — |
| Total assets | $ 168,636 | $ 168,636 | $ — | $ — |
| Liabilities: | | | | |
| Convertible Grant Agreement | $ 1,304 | $ — | $ — | $ 1,304 |
| Total liabilities | $ 1,304 | $ — | $ — | $ 1,304 |

| | December 31, 2023 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| Assets: | | | | |
| Cash equivalents - money market funds | $ 82,483 | $ 82,483 | $ — | $ — |
| Total assets | $ 82,483 | $ 82,483 | $ — | $ — |
| Liabilities: | | | | |
| Preferred stock warrant liability | $ 1,352 | $ — | $ — | $ 1,352 |
| Total liabilities | $ 1,352 | $ — | $ — | $ 1,352 |

The Company classifies its money market funds, which are valued based on quoted market prices in an active market with no valuation adjustment, as Level 1 assets within the fair value hierarchy. The Company's Convertible Grant Agreement is classified as Level 3 measurements under the fair value hierarchy as the fair values were determined based on significant inputs not observable in the market. See Note 8 for additional information on the Convertible Grant Agreement. See Note 14 for additional information regarding the valuation of the preferred stock warrant liability.

## 10. Asset Purchase and License Agreements

From time to time, the Company enters into asset purchase and license agreements with third parties. During the years ended December 31, 2024 and 2023, the Company was a party to the following significant agreements with certain financial commitments:

### Stanford License Agreement

On December 6, 2019, the Company entered into a license agreement with the Board of Trustees of the Leland Stanford Junior University ("Stanford") covering four inventions to guide treatment of psychiatry patients, some of which are jointly owned by other academic institutions but are exclusively managed by Stanford under certain invention management agreements between Stanford and the other institutions (the "Stanford License Agreement"). The Stanford License Agreement was subsequently amended in May 2020 and December 2023.

In connection with the Stanford License Agreement, as amended, the Company obtained an exclusive, worldwide, royalty-bearing license under certain patent rights in five patent families relating to brain stimulation, electroencephalogram and functional MRI that could be used to guide treatment of psychiatry patients (the "Stanford Licensed Patents"), and under certain technology relating to the inventions covered by the Stanford Licensed Patents (the "Stanford Licensed Technology"), to make, have made, use, sell, offer for sale and import licensed products for use in any indication. The Company's rights under the Stanford Licensed Patents are exclusive until December 2029, at which time it will become non-exclusive, and its rights under the Stanford Licensed Technology are non-exclusive. The Company may terminate the Stanford License Agreement at any time upon specified written notice to Stanford. Stanford may also terminate the agreement upon an uncured material breach of the agreement, including failure to achieved defined milestones related to the development and commercialization of the licensed products, as well as for certain other specified breaches.

As partial consideration to acquire these license rights, Alto paid a nominal upfront fee and reimbursed Stanford a nominal amount of prior patent prosecution expenses related to the licensed patents. Additionally, Alto is required to pay a low five-digit annual maintenance fee beginning on the first anniversary of the effective date through the term of the agreement. Alto also agreed to issue an aggregate of 71,370 shares of Alto's common stock, or 1% of Alto's equity on a fully-diluted basis, to Stanford and the other inventors. These shares were issued in April 2020. As additional consideration, the Company granted Stanford and the other inventors antidilution rights, whereby the Company agreed to maintain this collective equity ownership percentage at 1% until such time as the Company completed its initial qualified financing. In connection with this anti-dilution provision, Alto issued a further 32,978 shares of its common stock to Stanford and the other inventors in 2021. Following the initial closing of the Series A convertible preferred stock agreement, which met the definition of such qualified financing, the anti-dilution feature expired and no additional shares were issued.

In further consideration of the rights granted, beginning with the Company's first commercial sale of the licensed products, the Company will also pay an annual earned royalty in the very low single digits on net sales of licensed products, subject to certain customary reductions. The Company is also required to pay Stanford mid-teen to low-mid double digit percentages of any sublicensing consideration that it receives from third parties to whom the Company sublicenses rights under the Stanford Licensed Patents, depending on the timing of entry into the applicable sublicense. The Company does not have any future milestone payment obligations to Stanford or the other inventors under the Stanford License Agreement other than costs related to maintenance of patents.

### Sanofi License Agreement

Effective May 18, 2021, the Company entered into an agreement with Sanofi to obtain an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses, under certain patent rights and know-how of Sanofi relating to a PDE4 inhibitor compound, now known as ALTO-101, to use, develop, manufacture, commercialize or otherwise exploit ALTO-101 and products incorporating ALTO-101 in all human therapeutic, prophylactic and diagnostic uses. The Company also acquired a worldwide non-exclusive license to use certain know-how licensed to Sanofi by a specified third party to exploit the licensed products solely with respect to Parkinson's disease.

In exchange for the rights granted to the Company, the Company made a cash payment of $0.5 million which was recorded in research and development expenses during the year ended December 31, 2021 in the consolidated statements of operations and comprehensive loss since the acquired license does not have an alternative future use. The Company is

obligated to pay Sanofi up to an aggregate amount in the low-mid double digit millions upon the completion of a combination of development and regulatory approval milestones. If the Company achieves regulatory approval for one or more licensed products, the Company will owe Sanofi certain commercial milestone payments for the achievement of specified levels of aggregate, annual worldwide net sales of all licensed products, up to an aggregate amount of $102.0 million. In addition, if the Company grants sublicenses under the patents and know how licensed to the Company under the agreement, the Company will be required to pay sublicense revenue to Sanofi at tiered percentages ranging from low-mid double-digit percentages down to the very low double-digit percentages, reducing based on the time of entry into the applicable sublicense agreement. No additional milestones or royalties were paid or accrued during the years ended December 31, 2024 or 2023 related to this agreement.

In further consideration of the rights granted, beginning with the Company's first commercial sale of the licensed products, the Company will also pay an annual tiered earned royalty ranging from the mid-to-high single digits on net sales of licensed products, subject to certain customary reductions and a customary royalty floor. Royalties are payable, on a licensed products-by-licensed products and a country-by-country basis, until the latest to occur of (a) expiration of the last valid claim of a licensed patent covering such licensed products in such country, (b) the expiration of any regulatory exclusivity for such licensed products in such country, and (c) the 10th anniversary of the first commercial sale of such licensed product in such country. In addition, if the Company uses specified know-how licensed to Sanofi by the specified third party to exploit the licensed products for Parkinson's disease, the Company will be required pay an additional premium at a mid-single digit percentage on all fees, milestone payments and royalties payable by the Company to Sanofi under the agreement.

Unless terminated earlier, the license agreement with Sanofi will expire with respect to each licensed product, on a country-by-country basis, upon the expiration of the royalty term set forth above, and with respect to the agreement in its entirety upon the expiry of the royalty term for the last licensed product for which there has been a first commercial sale. Either the Company or Sanofi may terminate the Sanofi Agreement upon written notice for the uncured material breach of the other party. Sanofi also has the right to terminate the agreement for the Company's insolvency or if the Company brings or otherwise participates in a patent challenge against any licensed patents. The Company may terminate the agreement for any reason upon specified prior written notice to Sanofi.

**Cerecor License Agreement**

Effective May 28, 2021, the Company entered into an agreement with Cerecor Inc. (n/k/a Avalo Therapeutics, Inc.) ("Cerecor") to obtain an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses, under certain patent rights and know-how owned or controlled by Cerecor, relating to an NR2B inhibitor compound now known as ALTO-202, including certain rights licensed to Cerecor by Essex Chemie AG, or Merck, to research, develop, make, have made, use, import, offer for sale and sell ALTO-202 and products incorporating ALTO-202 ("Cerecor Licensed Products"), for the prevention, diagnosis and/or treatment of all diseases in humans.

In exchange for the rights granted to the Company, the Company made a cash payment of $0.5 million, which was recorded in research and development expenses during the year ended December 31, 2021 in the consolidated statements of operations and comprehensive loss since the acquired license does not have an alternative future use. The Company is obligated to make aggregate cash payments of up to $59.1 million per Cerecor Licensed Product if the Company achieves certain development, regulatory approval, and first commercial sale milestones for such Cerecor Licensed Product in up to a specified number of indications. If the Company successfully commercializes Cerecor Licensed Products, it will also be required to pay to Merck sales milestones totaling up to $15.0 million for all Cerecor Licensed Products, for the achievement of certain specified levels of worldwide annual aggregate net sales of all Cerecor Licensed Products. No additional milestones or royalties were paid or accrued during the years ended December 31, 2024 or 2023 related to this agreement.

In further consideration of the rights granted, beginning with the Company's first commercial sale of a Cerecor Licensed Product, the Company will also pay an annual tiered earned royalty in the high single digits in the aggregate on net sales of Cerecor Licensed Products. Royalties are payable, on a Cerecor Licensed Product-by-Cerecor Licensed Product and a country-by-country basis, until the later of the expiration of the last valid claim of a licensed patent covering such Cerecor Licensed Products in such country or 10 years after the first commercial sale of such Cerecor Licensed Product in such country. If the Company develops and commercializes a companion diagnostic as a standalone product in connection with a Cerecor Licensed Product, the Company will be required to make a one-time milestone payment to Cerecor upon the

achievement of a specified level of net sales of such companion diagnostic product, at an amount in the very low single digit millions.

The license agreement with Cerecor will terminate upon the expiration of the royalty term set forth above. Either the Company or Cerecor may terminate the Cerecor license agreement upon written notice for an uncured material breach of the other party, or in the case of an insolvency event of the other party. The Company may terminate the agreement for any reason upon specified prior written notice to Cerecor.

**Teva Asset Purchase Agreement**

Effective October 4, 2021, the Company entered into an agreement with Teva Pharmaceutical Industries, Ltd to acquire patents, know-how and other rights to ALTO-203 and a specified related compound (the "Teva Acquired Compound"), and assumed all post-acquisition liabilities related thereto.

In exchange for the rights granted to the Company, the Company made a cash payment of $0.5 million which was recorded in research and development expenses during the year ended December 31, 2021 in the consolidated statements of operations and comprehensive loss since the acquired license does not have an alternative future use. The Company is obligated to make aggregate cash payments of up to $27.0 million upon the achievement of certain development and regulatory approval milestones, and up to $35.0 million in the aggregate for the achievement of certain tiered sales milestones for any product that incorporates a Teva Acquired Compound (each, a "Teva Product"). In April 2024, the Company achieved a clinical milestone related to the initiation of its Phase 2 POC clinical trial evaluating ALTO-203, resulting in a cash payment of $0.5 million which was recorded in research and development expenses during the year ended December 31, 2024. No additional milestones or royalties were paid or accrued during the years ended December 31, 2024 or 2023 related to this agreement.

In further consideration of the rights granted, beginning with the Company's first commercial sale of a Teva Product, the Company will also pay an annual tiered earned royalty ranging from the mid-single-digits to 10 percent on net sales of Teva Products. Royalties are payable, on a Teva Product-by-Teva Product and a country-by-country basis, until the latest to occur of (a) expiration of the last valid claim of an acquired patent covering the composition of matter, or use or formulation of the composition of matter of a Teva Acquired Compound incorporated in or comprising such Teva Product in such country, (b) the expiration of new chemical entity data and/or market exclusivity for such Teva Product in such country or (c) the 10th anniversary of the date of first commercial sale of such Teva Product in such country.

**Palisade Asset Purchase Agreement**

Effective October 18, 2021, the Company entered into an agreement (the "Palisade Agreement") with Palisade Bio, Inc. ("Palisade") to acquire all patent, know-how and other rights to ALTO-100.

In exchange for the rights granted to the Company, the Company made a cash payment of $0.5 million which was recorded in research and development expenses during the year ended December 31, 2021 in the consolidated statements of operations and comprehensive loss since the acquired license does not have an alternative future use. The Company is obligated to make aggregate cash payments of up to $4.5 million upon the achievement of certain development and regulatory approval milestones. In connection with the sale or license by the Company to a third party of any of the patent, know-how or other rights included in the acquired assets prior to the achievement of a specified clinical development milestone, the Company will be required to pay to Palisade a low-double digit percentage of any consideration received by the Company from such license or sale, provided that the maximum aggregate consideration the Company will be required to pay to Palisade under the Palisade Agreement, including the upfront payment and all potential milestones and transaction-related payments, will not exceed $5.0 million. No additional milestones or royalties were paid or accrued during the years ended December 31, 2024 or 2023 related to this agreement.

**MedRx License Agreement**

On September 25, 2023, the Company entered into a joint development and license agreement (the "MedRx Agreement") with MedRx Co., Ltd. ("MedRx"), pursuant to which the Company obtained an exclusive, sublicensable, worldwide license, with the right to sublicense, under certain patent rights and know-how of MedRx relating to transdermal drug delivery to develop (excluding any pre-clinical development), manufacture, and commercialize transdermally delivered

pharmaceutical products comprising MedRx's transdermal patch technology and the Company's ALTO-101 (the "MedRx Licensed Products") for all therapeutic, prophylactic, and diagnostic uses. The Company granted MedRx an exclusive, sublicensable, worldwide license under certain patent rights and know-how relating to ALTO-101 owned or controlled by the Company, including certain patents and know how licensed to the Company pursuant to the Sanofi Agreement, solely to conduct pre-clinical development and manufacturing of the MedRx Licensed Products for the Company in accordance with the MedRx Agreement and a separate manufacturing and supply agreement to be entered into between the Company and MedRx. During the term of the MedRx Agreement, the Company agreed that it will not, directly or indirectly, develop, manufacture, or commercialize any pharmaceutical product that is a transdermal patch formulation containing similar active pharmaceutical ingredients as ALTO-101 and that is used in the same field and labeled for the same indications as the MedRx Licensed Products ("MedRx Competitive Product"). MedRx agreed that it will not, directly or indirectly, exploit any patch formulations of PDE4-inhibitor drugs for use within central nervous system disorders or exploit any MedRx Competitive Product, provided that if certain specified development or first commercial sale milestones are not achieved by certain specified dates, then MedRx has the right to cause the non-compete restrictions on both parties to lapse.

Under the MedRx Agreement, MedRx will be solely responsible for conducting all pre-clinical development of MedRx Licensed Products to support IND and institutional review board filing, and the Company will be solely responsible for all other development (including non-clinical studies and clinical studies) necessary to obtain regulatory approval for MedRx Licensed Products and subsequent commercialization of Products. The Company is obligated to use commercially reasonable efforts to commercialize MedRx Licensed Products in each of the following countries in which the Company has obtained regulatory approval: the United States; at least two of Germany, Spain, France, Italy or the United Kingdom; and one of China or Japan.

Pursuant to the MedRx Agreement, the Company paid MedRx an upfront fee of less than $0.2 million, which was recorded within research and development expenses during the year ended December 31, 2023 in the consolidated statements of operations and comprehensive loss since the acquired license does not have an alternative future use.

The Company is required to pay MedRx up to an aggregate of $11.0 million for the achievement of certain development and first commercial sale milestones for the first MedRx Licensed Product to achieve such milestones with respect to a first indication, and an additional milestone in the mid single digit millions for each additional approved distinct indication for such first MedRx Licensed Product or a subsequent MedRx Licensed Product. In April 2024, the Company achieved the desired pharmacokinetic profile for ALTO-101 in a Phase 1 trial, resulting in a milestone payment to MedRx comprised of $0.75 million, paid in cash, as well as 46,875 shares of the Company's common stock. The Company recognized $1.5 million of expense related to this milestone, which was recorded in research and development expenses in the consolidated statements of operations and comprehensive loss during the year ended December 31, 2024.

In addition, the Company will be required to pay MedRx sales milestones based on the achievement of specified thresholds of aggregate annual worldwide net sales of all MedRx Licensed Products of up to $110.0 million in the aggregate, if all such sales thresholds are achieved. Commencing on the first commercial sale of a MedRx Licensed Product, the Company will also be obligated to pay MedRx a mid-single digit royalty on annual, worldwide net sales of all MedRx Licensed Products, subject to certain customary reductions and a royalty floor. Royalties will be payable, on a MedRx Licensed Product-by-MedRx Licensed Product and country-by-country basis, until the latest to occur of (a) expiration of the last valid claim of certain specified patent rights covering such MedRx Licensed Products in such country, (b) the expiration of any regulatory exclusivity for such MedRx Licensed Product in such country, (c) the first approval of a specified generic product referencing such MedRx Licensed Product in such country, and (d) the tenth anniversary of the first commercial sale of such MedRx Licensed Product in such country, or the Royalty Term.

The MedRx Agreement will expire with respect to each MedRx Licensed Product, on a country-by-country basis, upon the expiration of the Royalty Term, and with respect to the entire MedRx Agreement upon the expiry of the last-to-expire Royalty Term for the last MedRx Licensed Product for which there has been a first commercial sale. Either the Company or MedRx may terminate the MedRx Agreement in its entirety or on a MedRx Licensed Product-by-MedRx Licensed Product basis upon an uncured material breach by the other party or in connection with an insolvency event of such party. In addition, if the Company or MedRx bring or otherwise participate in a patent challenge against any patents licensed by the other party, such other party may terminate the MedRx Agreement immediately. The Company has the right to terminate the MedRx Agreement in its entirety or on a MedRx Licensed Product-by-MedRx Licensed Product basis for any reason upon specified prior written notice to MedRx provided that the effective date of such termination will not be earlier than the completion date of a specified development event. The Company also has the right to terminate the MedRx

Agreement with respect to a MedRx Licensed Product immediately upon its reasonable determination of a material safety issue with respect to such MedRx Licensed Product. Except for the $1.5 million milestone discussed above, no additional milestones or royalties were paid or accrued during the years ended December 31, 2024 or 2023 related to this agreement.

## 11. Stock Based Plans

### *2024 Equity Incentive Plan*

In January 2024, the Board adopted, and the Company's stockholders approved, the 2024 Equity Incentive Plan (the "2024 Plan"), which became effective on the execution of the underwriting agreement related to the IPO. Under the 2024 Plan, the Company may grant incentive stock options to employees, including employees of any parent or subsidiary, and nonstatutory stock options, stock appreciation rights, RSAs, RSUs, performance awards and other forms of stock awards to employees, directors, and consultants, including employees and consultants of the Company's affiliates. The 2024 Plan is a successor to the 2019 Equity Incentive Plan, which was adopted by the Board of Directors in March 2019 (as amended, the "2019 Plan"). A total of 2,000,000 shares of common stock were approved to be initially reserved for issuance under the 2024 Plan. In addition, the number of shares of the Company's common stock reserved for issuance under the 2024 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2025 and continuing through and including January 1, 2034, in an amount equal to 5% of the total number of shares of the Company's common stock outstanding on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by the Board. On January 1, 2025, the number of shares of common stock reserved for issuance under the 2024 Plan increased by 1,349,328 shares. No future issuances were made under the 2019 Plan upon the effectiveness of the 2024 Plan.

As of December 31, 2024, the total number of shares authorized to be issued under the 2024 Plan was 2,000,000. As of December 31, 2023, the total number of shares authorized to be issued under the 2019 Plan was 4,078,285. As of December 31, 2024 there were 198 shares of common stock reserved and available for issuance under the 2024 Plan. As of December 31, 2023 there were 251,450 shares of common stock reserved and available for issuance under the 2019 Plan.

### *Employee Stock Purchase Plan*

In January 2024, the Board adopted, and the Company's stockholders approved, the 2024 Employee Stock Purchase Plan (the "ESPP"), which became effective on the execution of the underwriting agreement related to the IPO. A total of 250,000 shares of common stock were approved to be initially reserved for issuance under the ESPP. In addition, the number of shares of common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year, beginning on January 1, 2025 and continuing through, and including, January 1, 2034, by the lesser of (1) 1% of the total number of shares of the Company's common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (2) 750,000 shares; provided, that before the date of any such increase, the Board may determine that such increase will be less than the amount set forth in clauses (1) and (2). On January 1, 2025, the number of shares of common stock reserved for issuance under the ESPP increased by 269,865 shares. As of December 31, 2024, the Company had not opened the ESPP for enrollment, and therefore there were no purchases or share issuances during this period.

### Stock Options

The options have a 10-year life and generally vest over a period of four years, with the first 25% of the award vesting after one year and then monthly thereafter, subject to continuous service. Once the options are exercised, the shares are subject to transfer restrictions under the terms of the Company's amended and restated certificate of incorporation.

The fair value of each option award is estimated using the Black-Scholes option-pricing model which involves the use of certain subjective assumptions. These assumptions and estimates are as follows:

*Fair Value of Common Stock.* As the Company's common stock was not publicly traded prior to its IPO, the fair value was determined by the Board, with input from management and valuation reports prepared by independent third-party valuation firms. After the completion of the Company's IPO, the fair value of common stock is based on the closing price of the Company's common stock on the New York Stock Exchange as reported on the date of the grant.

*Risk-Free Interest Rate*. The risk-free interest rate for the expected term of the options was based on the U.S. Treasury yield curve in effect at the time of the grant.

*Expected Term*. The expected term of options represents the period of time that options are expected to be outstanding. The Company's historical stock option exercise experience does not provide a reasonable basis upon which to estimate an expected term due to a lack of sufficient data. The Company estimated the expected term by using the simplified method, using the average of the time-to-vesting and the contractual life of the options.

*Expected Volatility*. As the Company does not have sufficient trading history to estimate the volatility of its common stock, the expected volatility was estimated by taking the average historic price volatility for industry peers, consisting of several public companies in the Company's industry which are either similar in size, stage of life cycle, or financial leverage, over a period equivalent to the expected term of the awards, where available.

*Expected Dividend Yield*. The Company has never declared or paid any cash dividends and do not presently plan to declare or pay cash dividends in the foreseeable future. As a result, an expected dividend yield of zero percent was used.

The weighted-average grant date fair value of options granted during 2024 and 2023 for awards subject only to service-based vesting conditions were $9.50 and $4.85 per share, respectively, which were based on the following weighted-average assumptions:

| | 2024 | 2023 |
|---|---|---|
| Exercise price | $ 12.38 | $ 5.82 |
| Fair value of common stock | $ 12.38 | $ 6.23 |
| Expected term (in years) | 6.0 | 6.0 |
| Volatility | 90.5% | 92.0% |
| Risk free rate | 4.1% | 3.8% |
| Dividend yield | 0% | 0% |

The table below summarizes activity related to stock options subject only to service-based vesting conditions (amounts in thousands, except per share amounts):

| | Shares | Weighted – average exercise price ($) | Weighted – average remaining contractual term (in years) | Aggregate intrinsic value ($) |
|---|---|---|---|---|
| Outstanding at December 31, 2022 | 1,680 | $ 3.67 | 8.6 | $ 4,307 |
| Granted | 1,585 | 5.82 | | |
| Exercised | (68) | 2.66 | | 216 |
| Forfeited and cancelled | (317) | 5.86 | | |
| Outstanding at December 31, 2023 | 2,880 | 4.48 | 8.7 | 7,794 |
| Granted | 2,142 | 12.38 | | |
| Exercised | (125) | 1.50 | | 368 |
| Forfeited and cancelled | (382) | 9.58 | | |
| Outstanding at December 31, 2024 | 4,515 | 7.88 | 8.3 | 2,109 |
| Exercisable at December 31, 2024 | 1,532 | 4.48 | 6.9 | 1,790 |

As of December 31, 2024, there was approximately $19.9 million of unrecognized stock-based compensation expense related to these service-based unvested stock options which is expected to be recognized over a weighted-average period of 2.9 years.

***Restricted Stock Units***

The table below summarizes activity related to RSUs subject only to service-based vesting conditions (in thousands, except per share amounts):

| | Shares | Weighted-average grant date fair value per share |
|---|---|---|
| Outstanding, December 31, 2023 | — | $ — |
| Granted | 54 | 14.88 |
| Vested | — | — |
| Forfeited and cancelled | — | — |
| Outstanding, December 31, 2024 | 54 | $ 14.88 |

On March 1, 2024, the Company issued 53,864 RSUs under the 2024 Plan; 50% of the shares of common stock underlying the RSUs vest after 18 months and the remainder vest after 24 months from the grant date. The RSUs are subject only to a service-based vesting condition. Such shares are not accounted for as outstanding until they vest. As of December 31, 2024, the total unrecognized compensation related to unvested RSUs granted was $0.5 million which is expected to be amortized on a straight-line basis over the weighted-average remaining vesting period of approximately 1.2 years.

**Performance Option Awards**

The Board granted options to purchase common stock to certain employees and consultants that vest upon the achievement of certain performance conditions ("Performance Awards"), such as the completion of a future financing event or upon the achievement of defined clinical milestones or outcomes. During the year ended December 31, 2023, the Company issued 194,835 Performance Awards with an exercise price of $5.30 per share. The Performance Awards have a contractual term of ten years. The aggregate grant date fair value of the Performance Awards granted during the years ended December 31, 2023 is $0.9 million. The Company did not issue Performance Awards during the year ended December 31, 2024.

During the years ended December 31, 2024 and 2023, financing and clinical milestones were met, which resulted in the vesting of 194,835 shares and 187,714 Performance Awards, respectively and the recognition of $0.9 million and $0.9 million of stock-based compensation expense, respectively. As of December 31, 2024, there were 592,748 Performance Awards still outstanding, with a weighted-average exercise price of $4.63 per share, of which none remain unvested. The remaining contractual life of the Performance Awards was 7.8 years as of December 31, 2024. There is no unrecognized stock-based compensation expense related to these Performance Awards as of December 31, 2024.

**Stock-based Compensation Expense**

Non-cash stock-based compensation expense recognized in the accompanying consolidated statements of operations and comprehensive loss for the years ended December 31, 2024 and 2023 was as follows (in thousands):

| | 2024 | 2023 |
|---|---|---|
| Research and development | $ 3,631 | $ 2,166 |
| General and administrative | 4,000 | 725 |
| Total stock-based compensation expense | $ 7,631 | $ 2,891 |

**Restricted Stock Awards**

In June 2020, the Company granted a restricted stock award of 202,329 common shares to the Company's Chief Executive Officer with a grant date fair value per share of $0.58. The restricted stock award vests over four years, or upon a change in the control of the Company, subject to continued employment with the Company. In the event of a change in control, the unvested restricted stock award will be accelerated and fully vested immediately prior to the change in control. There are no performance-based features or market conditions associated with this award. The fair value of the restricted stock award is determined based on the number of restricted shares granted and the fair value of the Company's stock on the date of

grant. The Company issued this award in exchange for cash proceeds of approximately $0.1 million, which was representative of the fair value of the shares at the grant date, and therefore there was no stock-based compensation expense associated with this equity award. As of December 31, 2024 and 2023, there were zero and 21,075 shares of unvested restricted stock outstanding, respectively.

## 12. Loss Per Share

Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period. The Company's unvested restricted common stock is not included in the determination of loss per share until the award vests. Diluted net loss per common share excludes the potential impact of the Company's convertible preferred stock and warrants because their effect would be anti-dilutive due to the Company's net loss. Since the Company had a net loss in each of the periods presented, basic and diluted net loss per common share are the same.

The following outstanding potentially dilutive common stock equivalents were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Convertible preferred stock (as if converted) | — | 13,664 |
| Preferred stock warrants | — | 245 |
| Common stock warrants | 36 | — |
| Restricted common stock units and awards | 54 | 21 |
| Stock options issued and outstanding | 5,108 | 3,471 |
| Total | 5,198 | 17,401 |

## 13. Income Taxes

### Provision for Income Taxes

There is no provision for income taxes because the Company has historically incurred operating losses and maintains a full valuation allowance against its net deferred tax assets. In 2024 and 2023, substantially all of the Company's net losses were generated in the United States.

The effective tax rate of the Company's provision (benefit) for income taxes differs from the U.S. federal statutory rate as follows:

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Statutory rate | 21.0% | 21.0% |
| State taxes, net of federal tax benefit | (0.5%) | 6.2% |
| Research and development tax credits | 2.5% | 2.8% |
| Change in valuation allowance | (23.4)% | (30.3)% |
| Other | 0.4 % | 0.3% |
| Income tax provision (benefit) | 0.0% | 0.0% |

### Deferred Tax Assets and Valuation Allowance

Deferred tax assets reflect the tax effects of net operating losses ("NOLs"), and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The most significant item of deferred tax assets is derived from the Company's federal NOLs.

The most significant components of the Company's deferred tax assets (liabilities) are as follows (in thousands):

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| Deferred tax assets: | | |
| Net operating loss carryforwards | $ 12,124 | $ 10,570 |
| Stock-based compensation | 1,975 | 319 |
| R&D deferred costs | 17,364 | 9,019 |
| Accrued expenses and other, net | 2,064 | 1,085 |
| Tax credit carryforwards | 4,331 | 2,172 |
| Lease liability | 1,507 | — |
| Total deferred tax assets | 39,365 | 23,165 |
| Less: valuation allowance | (37,400) | (23,019) |
| Net deferred tax assets | 1,965 | 146 |
| Deferred tax liabilities: | | |
| Right of use lease asset | (1,409) | — |
| Fixed assets | (556) | (146) |
| Total deferred tax liabilities | $ (1,965) | $ (146) |
| Net deferred taxes | $ — | $ — |

A valuation allowance is provided when it is more likely than not that the deferred tax assets will not be realized. The Company has established a valuation allowance to offset the gross deferred tax assets as of December 31, 2024 and 2023 due to the uncertainty of realizing future tax benefits from its NOL carryforwards and other deferred tax assets. The valuation allowance increased by $14.4 million and $11.2 million during the years ended December 31, 2024 and 2023, respectively.

At December 31, 2024, the Company had U.S. federal gross NOL carryforwards of $42.2 million, state gross NOL carryforwards of $33.6 million, foreign gross NOL carryforwards of $3.0 million, and tax credit carryforwards of $4.3 million. State NOL carryforwards begin to expire in 2039 and tax credit carryforwards will begin to expire in 2042 with $0.1 million of tax credit carryforwards having no expiration. US federal and foreign gross NOL carryforwards have no expiration.

The Company's NOL and tax credit carryforwards could be subjected to a limitation pursuant to a cumulative change in substantial ownership as identified in Sections 382 and 383 of the Internal Revenue Code and similar state provisions. These ownership changes may limit the amount of NOL and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company completed a study and determined that historical changes, under Section 382 and 383, have occurred and as a result approximately $24.0 million of the NOLs and tax credits carryforwards are subjected to the limitation. These related gross federal NOLs are subject to a full valuation allowance as of December 31, 2024. The Company will continue to monitor equity movement and its impact on the utilization of the NOLs and credits as the Company could experience subsequent ownership changes which may result in additional limitations on the utilization of NOL and credit carryforwards.

The Company is subject to income taxes in the U.S. federal jurisdiction, various state and local jurisdictions and in one foreign tax jurisdiction. The Company's tax years from inception through 2024 are subject to examination by the U.S., state, and foreign tax authorities due to the carryforward of unutilized NOLs and research and development credits. The Company is not currently under examination in any tax jurisdictions.

## 14. Common Stock, Convertible Preferred Stock and Preferred Stock Warrants

Upon closing of the IPO in February 2024, all of the outstanding convertible preferred stock automatically converted into 13,664,261 shares of common stock. Subsequent to the closing of the IPO, there were no shares of convertible preferred stock outstanding.

At December 31, 2023, convertible preferred stock consisted of the following (amounts in thousands, except per share amounts):

| Share Class | Shares Authorized | Shares Issued and Outstanding | Issuance Price per Share | Carrying Value | Liquidation Preference |
|---|---|---|---|---|---|
| Series Seed Preferred | 3,709 | 3,709 | $ 2.0822 | $ 7,674 | $ 7,722 |
| Series A Preferred | 7,251 | 6,785 | $ 4.6996 | 30,489 | 31,887 |
| Series B Preferred | 9,877 | 9,877 | $ 6.0000 | 58,918 | 62,095 |
| Series C Preferred | 10,675 | 9,548 | $ 4.7132 | 44,396 | 45,000 |
| Total | 31,512 | 29,919 | | $ 141,477 | $ 146,704 |

### Series Seed Preferred Stock

On September 13, 2019, the Company entered into a purchase agreement, as amended, with a number of investors for a private placement of 3,708,682 shares of Series Seed Preferred Stock. The Series Seed Preferred Stock was sold at a price of $2.0822 per share for gross proceeds of $7.7 million. The shares were issued across multiple dates between late 2019 and early 2020 for the same price per share.

### Series A Preferred Stock

On May 3, 2021, the Company entered into a purchase agreement (the "Series A Purchase Agreement") with a number of investors for a private placement of 6,785,075 shares of Series A Preferred Stock. The Series A Preferred Stock was sold at a price of $4.6996 per share for gross proceeds of $31.9 million. The shares were issued across multiple dates between May and August 2021 for the same price per share.

### Series B Preferred Stock

On April 6, 2022, the Company entered into a purchase agreement, as amended, with a number of investors, including a majority investor party to the Series A Purchase Agreement, for a private placement of 3,512,787 shares of Series B Preferred Stock. The Series B Preferred Stock was sold at a price of $6.00 per share for gross proceeds of $21.1 million. Following the initial close of the Series B Preferred Stock, additional closings occurred throughout 2022 which resulted in the sale of an incremental 2,197,501 shares of Series B Preferred Stock at the same price per share for gross proceeds of $13.2 million. In January 2023, the Company sold 4,166,667 shares of Series B Preferred Stock to a new investor for gross proceeds of $25.0 million.

In January 2023, the Board approved a 1.1156 for 1 forward stock split of the Company's issued and outstanding shares of Series B Preferred Stock, and a proportional adjustment to the existing conversion ratio, as well as the exercise price of the then-outstanding K2 Warrant. Accordingly, all Series B share and per share amounts for all periods presented in the financial statements have been adjusted retroactively, where applicable, to reflect this stock split and adjustment of the preferred stock conversion ratio.

### Series C Preferred Stock

On November 20, 2023, the Company entered into a purchase agreement (the "Series C Purchase Agreement"), pursuant to which the Company sold 9,547,802 shares of Series C convertible preferred stock at a price of $4.7132 per share for gross proceeds of $45.0 million. The majority of investors that participated in the Series C Purchase Agreement were new investors.

In connection with the closing of the Series C Purchase Agreement, the Board authorized an increase to the number of authorized shares of common stock to 52,000,000.

**Preferred Stock Warrants**

*Series A Preferred Stock Warrants*

In May 2021, in connection with the closing of the Series A Preferred Stock Agreement, the Company issued warrants to the lead Series A investor to purchase an aggregate of 465,917 shares of Series A Preferred Stock ("Series A Preferred Stock Warrants") at a price of $4.6996 per share ("Exercise Price"). The Series A Preferred Stock Warrants expire, and if not earlier exercised, will be automatically net exercised, on the earliest to occur of (i) the closing of a deemed liquidation event; (ii) the closing of the sale of shares of common stock in a public offering resulting in at least $75.0 million of gross proceeds and a share price of at least $15.68 per share (one and one half times the Exercise Price as adjusted by the reverse stock split discussed in Note 2); (iii) immediately prior to the consummation of a SPAC transaction in which the combined company, immediately following the closing of the SPAC transaction, holds at least $75.0 million in unrestricted cash; or (iv) May 3, 2026. The Company completed its IPO in February 2024 at $16.00 per share, resulting in a net exercise of the Series A Preferred Stock Warrants.

The Company determined the estimated fair value of the Series A Preferred Stock Warrants at the date of issuance to be $1.2 million, which was derived using weighted outcomes. As of December 31, 2023, the Company remeasured the fair value of the Series A Preferred Stock Warrants where the significant assumptions included an expected life of 2 years, a risk free rate of 4.5% and an expected volatility of 99%. The remeasured fair value of the Series A Preferred Stock Warrants resulted in a non-cash gain of $0.5 million during the year ended December 31, 2023.

In February 2024, in connection with the IPO, the Series A Preferred Stock Warrants were exercised and net settled for shares of the Company's common stock, which resulted in the issuance of 72,631 shares of common stock. The Company remeasured the fair value of the Series A Preferred Stock Warrants immediately prior to their exercise, resulting in an insignificant change in fair value during the year ended December 31, 2024. The resulting warrant liability was then extinguished upon the net exercise.

*K2 Warrant*

In December 2022, in connection with the closing of the Loan Agreement, the Company issued a warrant to the Lender to purchase a number of shares of the Company's Series B convertible preferred stock, or at Lender's election, next round stock ("K2 Warrant"). The number of shares of convertible preferred stock issuable upon exercise of the warrant is equal to (a) (i) 0.0375, multiplied by (ii) the aggregate principal amount of term loans actually funded under the Loan Agreement, divided by (b) the warrant price then in effect. Following the sale and issuance of the Series C Preferred Stock in November 2023 and as of December 31, 2023, the exercise price of the warrants is $4.7132 per share, which would result in the issuance of an aggregate of 79,564 shares of Series C Preferred Stock. Following the conversion of Series C Preferred Stock to common stock upon the completion of the IPO in February 2024, the K2 Warrant became a warrant to purchase up to an aggregate of 35,773 shares of the Company's common stock at an exercise price of $10.49 per share. The K2 Warrant was remeasured to fair value immediately prior to the conversion to a common stock warrant, and the change in fair value since December 31, 2023 was $0.2 million. The Company determined that the K2 Warrant is equity-classified, and therefore the resulting warrant liability was reclassified to permanent equity, and is not subject to future remeasurement. On January 13, 2025, the Company amended the Loan Agreement and the K2 Warrant. See Note 18 for additional information.

The following table summarizes the change in fair value of the preferred stock warrant liability, a Level 3 recurring fair value measurement, for the years ended December 31, 2024 and 2023 (in thousands):

| | Preferred Stock Warrant Liability |
|---|---|
| Balance at December 31, 2022 | $ 1,877 |
| Issuance | — |
| Exercise | — |
| Expiration | — |
| Change in fair value | (525) |
| Balance at December 31, 2023 | 1,352 |
| Issuance of Preferred Stock Warrants | — |
| Exercise | — |
| Expiration | — |
| Change in fair value | 243 |
| Balance at February 2, 2024 | 1,595 |
| Reclassification to equity (1) | (1,595) |
| Balance at December 31, 2024 | $ — |

(1) Following the Company's IPO, the warrant liability was reclassified to equity.

**Common Stock and Authorized Shares**

As of December 31, 2024 and 2023, the Company had 500,000,000 and 52,000,000 authorized shares of common stock, respectively, with a par value of $0.0001 per share, of which 26,986,560 and 3,832,134 shares, respectively, were legally issued and outstanding. On February 6, 2024, the Company amended its certificate of incorporation such that the total number of shares of common stock authorized to be issued was increased to 500,000,000, and the total number of shares of new preferred stock authorized to be issued was 10,000,000 with a par value per share of $0.0001. As of December 31, 2024, no shares of preferred stock were issued or outstanding.

As of December 31, 2024 and 2023, the Company had reserved common stock, on an as-if converted basis, for issuance as follows (in thousands):

| | December 31, 2024 | 2023 |
|---|---|---|
| Series Seed Preferred Stock | — | 1,668 |
| Series A Preferred Stock | — | 3,051 |
| Series B Preferred Stock | — | 4,653 |
| Series C Preferred Stock | — | 4,293 |
| Series A Preferred Stock Warrants | — | 209 |
| K2 Warrant | 36 | 36 |
| Stock options issued and outstanding | 5,108 | 3,471 |
| Stock options available for future grant | — | 251 |
| Total | 5,144 | 17,632 |

**15. Commitments and Contingencies**

From time to time, the Company is subject to occasional lawsuits, investigations and claims arising out of the normal conduct of business. The Company has no significant pending or threatened litigation as of December 31, 2024.

In the normal course of business, the Company enters into contracts that contain a variety of indemnifications with its employees, licensors, suppliers, and service providers. Further, the Company indemnifies its directors and officers who are, or were, serving at the Company's request in such capacities. The Company's maximum exposure under these arrangements is unknown at December 31, 2024. The Company does not anticipate recognizing any significant losses relating to these arrangements.

## 16. Retirement Plan

The Company has established a defined contribution 401(k) plan (the "401(k) Plan") for the benefit of its employees. All of the full-time employees of the Company are eligible to participate in the 401(k) Plan which permits employees to make voluntary contributions up to the dollar limit allowed under the Internal Revenue Code. The 401(k) Plan also provides for matching contributions as defined by the Company of up to a combined total of 3% of an employee's eligible annual compensation. The Company recorded matching contributions of $0.3 million and $0.2 million for the years ended December 31, 2024 and 2023, respectively.

## 17. Segments

The Company's operations are managed and reported to its President and CEO, the Company's CODM, on a consolidated basis. The Company is a clinical-stage biopharmaceutical company advancing psychiatry through its proprietary Precision Psychiatry Platform, which leverages advanced data science and neurobiology to develop personalized treatments. The CODM assesses performance and allocates resources based on the Company's consolidated net loss, as the integrated approach to neurobiologically driven drug development requires the CODM to manage and evaluate the results of the business in a consolidated manner to drive efficiencies and develop uniform strategies. Accordingly, key components and processes of the Company's operations are managed centrally, including clinical studies and personnel. Asset information is not used by the CODM to allocate resources. Under this organizational and reporting structure, the Company has one reportable segment.

As a single reportable segment entity, the Company's segment performance measure is consolidated net loss. Certain significant segment expenses below loss from operations are presented in the Company's consolidated statements of operations and are therefore not presented below. Additional disaggregated significant segment expenses on a functional basis, that are not separately presented on the Company's consolidated statements of operations, are presented below:

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Personnel expenses excluding stock-based compensation | $ 20,851 | $ 13,377 |
| Stock-based compensation | 7,631 | 2,891 |
| Direct external program expenses: | | |
| ALTO-100 | 7,371 | 7,748 |
| ALTO-300 | 6,410 | 3,070 |
| ALTO-101 | 2,798 | 1,731 |
| ALTO-203 | 3,672 | 222 |
| Other research and development [(a)] | 7,810 | 4,387 |
| General and administrative [(b)] | 12,067 | 4,383 |
| Loss from operations | $ 68,610 | $ 37,809 |

(a) Other research and development expenses primarily consists of license fees, facility charges, third party consultant costs, early research costs related to other product candidates, and other unallocated costs.
(b) General and administrative costs include professional fees, insurance, consultant fees and facility charges.

## 18. Subsequent Events

*Equity Grants*

Across January, February and March 2025, the Company granted options for the purchase of 0.8 million shares of common stock at a weighted-average exercise price of $4.21, which are expected to vest over a weighted average term of 3.7 years.

*Amended Loan Agreement*

In January 2025, the Company amended the Loan Agreement (as amended, the "Amended Loan Agreement") to, among other things, extend the Term Loan (as defined below) maturity date and increase the maximum available amount of term loans. The Amended Loan Agreement provides for up to an aggregate term loan in the principal amount of $75.0 million ("Term Loan"), consisting of a first tranche term loan of $20.0 million, a second tranche term loan of up to an additional $30.0 million available at the Company's request until December 15, 2025, subject to certain time-based, clinical milestones, and an additional third tranche term loan of up to an additional $25.0 million available at the Company's request subject to the Lender's approval. The Company drew $20.0 million upon entry into the Amendment (approximately $10.0 million of which was used to refinance obligations under the Original Loan Agreement and pay fees and expenses incurred in connection with the Amendment).

As of December 31, 2024, the Company had an outstanding principal balance of $10.0 million under the Original Loan Agreement. As of the date of the Amendment, and following the related refinancing, the Company had an outstanding principal balance of $20.0 million under the Term Loan. Since the principal amounts due within one year from the balance sheet have been refinanced on a long-term basis after the balance sheet date but before the issuance of these financial statements, the entire amount funded under the Loan Agreement has been classified as non-current as of December 31, 2024.

The Term Loan matures on January 1, 2029. The Amended Loan Agreement provides for an interest only period until January 1, 2027, which may be extended to January 1, 2028, subject to the funding of at least $20.0 million of the second tranche term loan, following which the Term Loan shall be repaid in equal monthly payments through the Term Loan maturity date.

Borrowings under the Amended Loan Agreement bear interest at (i) a variable per annum cash pay rate equal to the Prime Rate plus 1.45% (subject to a floor of 8.45% per annum) and (ii) a fixed per annum paid-in-kind rate equal to 1.0%. Interest is due and payable monthly in arrears. Upon final payment or prepayment of the Term Loan, the Company is required to pay a final payment equal to 5.95% of the amount borrowed.

The Company's obligation under the Original Loan Agreement to pay the Lender a one-time fee of $625,000 on the earlier of December 1, 2026 or earlier prepayment of the Term Loan remains outstanding.

*Loan Conversion Feature*: Under the terms of the Amended Loan Agreement, the Lender may, at its option, elect to convert up to $9.0 million of the then outstanding Term Loan (the "Conversion Amount") ($4.0 million of which was reflected in the Original Loan Agreement and $5.0 million of which is reflected in the Amendment) into shares of the Company's common stock (the "Conversion Shares"). The number of shares to be issued upon conversion is determined by dividing (a) the portion of the term loan amount converted, by (b) the Applicable Conversion Price. Applicable Conversion Price means (i) with respect to any conversion of up to $4.0 million of the Conversion Amount, $10.49, and (ii) with respect to any conversion of the remaining $5.0 million of the Conversion Amount, $4.8259, in each case subject to certain adjustments set forth in the Amended Loan Agreement.

*Warrants*: In connection with the Original Loan Agreement, the Company issued to the Lender a warrant (the "Original Warrant"), which Original Warrant is exercisable for 35,773 shares of the Company's common stock and expires on December 15, 2032. In connection with the Amendment, the Original Warrant was amended and restated (the "Amended and Restated Warrant") to lower the exercise price to $3.7122 per share (the "Exercise Price"). Further, in connection with the Amendment, the Company issued an additional warrant (the "New Warrant", together with the Amended and Restated Warrant, the "Warrants") to purchase a number of shares of the Company's common stock calculated as follows: (a) (i) 0.025, multiplied by (ii) the aggregate principal amount of the term loans actually funded under the Amended Loan Agreement, divided by (b) the Exercise Price. The New Warrant expires on January 13, 2035. The exercise of the Warrants is subject to the same beneficial ownership and overall share issuance limitations set forth above under "Loan Conversion Feature."

The Company is continuing to evaluate the accounting for the Amended Loan Agreement to determine whether the transaction should be accounted for as a debt modification or a loss on debt extinguishment.

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

None.

**Item 9A. Controls and Procedures.**

***Evaluation of Disclosure Controls and Procedures***

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported, within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure. Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this report, the effectiveness of 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 principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

***Management's Annual Report on Internal Control over Financial Reporting***

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting. Management conducted an assessment of our internal control over financial reporting based on the Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that assessment, management has concluded that, as of December 31, 2024, our internal control over financial reporting was effective.

This Annual Report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Pursuant to the SEC rules, because we qualify as an emerging growth company under the JOBS Act, management's report was not subject to attestation by our independent registered public accounting firm.

***Changes in Internal Control over Financial Reporting***

There was no change in our internal control over financial reporting that occurred during the quarter ended December 31, 2024 that has materially affected or is reasonably likely to materially affect our internal control over financial reporting.

***Limitations on Effectiveness of Controls and Procedures***

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the company have been detected. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

**Item 9B. Other Information.**

None.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.**

Not applicable.

## Part III

### Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with our 2025 Annual Meeting of Stockholders, or the Proxy Statement, which is expected to be filed no later than 120 days after the end of our fiscal year ended December 31, 2024, under the headings "Board of Directors and Corporate Governance," "Election of Directors," "Executive Officers" and "Insider Trading Policy" and is incorporated herein by reference. A copy of our Insider Trading Policy is filed as Exhibit 19.1 to this Annual Report.

*Code of Business Conduct and Ethics*

We have adopted a written code of business conduct and ethics, or the Code of Conduct, that applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or person performing similar functions. A copy of the Code of Conduct is available in the investors section of our website at www.altoneuroscience.com. We intend to disclose on our website any future amendments of our Code of Conduct or waivers that exempt any of the principal executive officer, principal financial officer, principal accounting officer or controller, persons performing similar functions or our directors from provisions in the Code of Conduct. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report.

### Item 11. Executive Compensation.

The information required by this item will be contained in our Proxy Statement which is expected to be filed no later than 120 days after the end of our fiscal year ended December 31, 2024, under the headings "Executive Compensation," and "Non-Employee Director Compensation" and is incorporated herein by reference.

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

The information required by this item will be contained in our Proxy Statement which is expected to be filed no later than 120 days after the end of our fiscal year ended December 31, 2024, under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans" and is incorporated herein by reference.

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

The information required by this item will be contained in our Proxy Statement which is expected to be filed no later than 120 days after the end of our fiscal year ended December 31, 2024, under the headings "Transactions with Related Persons and Indemnification" and "Independence of the Board of Directors" and is incorporated herein by reference.

### Item 14. Principal Accountant Fees and Services.

The information required by this item will be contained in our Proxy Statement which is expected to be filed no later than 120 days after the end of our fiscal year ended December 31, 2024, under the headings "Ratification of Selection of Independent Registered Public Accounting Firm" and is incorporated herein by reference.

## Part IV

### Item 15. Exhibits and Financial Statement Schedules.

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

(1) **Financial Statements**

See Index to Financial Statements under Part II, Item 8 of this Annual Report.

(2) **Financial Statement Schedules**

Schedules not listed above have been omitted because they are not required, not applicable, or the required information is otherwise included.

(3) **Exhibits**

| Exhibit No. | Description | Form | File No. | Exhibit | Filing Date | Filed Herewith |
|---|---|---|---|---|---|---|
| 1.1 | Sales Agreement, by and between the Company and Leerink Partners LLC, dated as of February 3, 2025 | S-3 | 333-284667 | 1.2 | 2/3/2024 | |
| 3.1 | Amended and Restated Certificate of Incorporation of the Registrant | 8-K | 001-41944 | 3.1 | 2/6/2024 | |
| 3.2 | Amended and Restated Bylaws of the Registrant | 8-K | 001-41944 | 3.2 | 2/6/2024 | |
| 4.1 | Form of Common Stock Certificate | S-1/A | 333-276495 | 4.1 | 1/29/2024 | |
| 4.2† | Amended and Restated Investor Rights Agreement, by and among the Registrant and certain of its stockholders, dated as of November 20, 2023 | S-1 | 333-276495 | 4.2 | 1/12/2024 | |
| 4.3 | Amended and Restated Warrant to Purchase Stock, dated January 13, 2025, issued to K2 HealthVentures Equity Trust LLC | 8-K | 001-41944 | 4.1 | 1/16/2025 | |
| 4.4 | Warrant to Purchase Stock, dated January 13, 2025, issued to K2 HealthVentures Equity Trust LLC | 8-K | 001-41944 | 4.2 | 1/16/2025 | |
| 4.5 | Description of Securities | | | | | X |
| 10.1+ | 2019 Equity Incentive Plan | S-1 | 333-276495 | 10.1 | 1/12/2024 | |
| 10.2+ | Form of Option Grant Notice and Agreement, Exercise Notice, Early Exercise Notice, and Restricted Award Notice under the 2019 Equity Incentive Plan | S-1 | 333-276495 | 10.2 | 1/12/2024 | |
| 10.3+ | 2024 Equity Incentive Plan | S-1/A | 333-276495 | 10.3 | 1/29/2024 | |
| 10.4+ | Form of Option Grant Notice and Agreement, and Exercise Notice under the 2024 Equity Incentive Plan | S-1/A | 333-276495 | 10.4 | 1/29/2024 | |
| 10.5+ | Form of RSU Award Grant Notice and Agreement under the 2024 Equity Incentive Plan | S-1/A | 333-276495 | 10.5 | 1/29/2024 | |

| Exhibit No. | Description | Form | File No. | Exhibit | Filing Date | Filed Herewith |
|---|---|---|---|---|---|---|
| 10.6+ | 2025 Inducement Plan | | | | | X |
| 10.7+ | Form of Option Grant Notice and Agreement, and Exercise Notice under the 2025 Inducement Plan | | | | | X |
| 10.8+ | 2024 Employee Stock Purchase Plan | S-1/A | 333-276495 | 10.6 | 1/29/2024 | |
| 10.9+ | Non-Employee Director Compensation Policy | | | | | X |
| 10.10+ | Form of Indemnification Agreement between the Registrant and each of its directors and executive officers | S-1/A | 333-276495 | 10.7 | 1/29/2024 | |
| 10.11+ | Form of Employment Offer Letter for executive officers | S-1 | 333-276495 | 10.8 | 1/12/2024 | |
| 10.12+ | Form of Amendment to Employment Offer Letter | S-1/A | 333-276495 | 10.9 | 1/29/2024 | |
| 10.13† | Loan and Security Agreement, by and among the Registrant, K2 HealthVentures LLC, as a lender, and the other lenders from time to time party thereto, or collectively the Lender, K2 HealthVentures LLC, as administrative agent for the Lender, and Ankura Trust Company, LLC, as collateral agent for the Lender, dated as of December 16, 2022 | S-1 | 333-276495 | 10.9 | 1/12/2024 | |
| 10.14† | First Amendment to Loan and Security Agreement, by and among the Registrant, K2 HealthVentures LLC, as lender, K2 HealthVentures LLC, as administrative agent for the Lender, and Ankura Trust Company, LLC, as collateral trustee for the Lender, dated as of January 13, 2025 | 8-K | 001-41944 | 10.1 | 1/16/2025 | |
| 10.15# | Exclusive License Agreement With Equity, by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated as of December 6, 2019, as amended as of May 18, 2020 and December 11, 2023 | S-1 | 333-276495 | 10.10 | 1/12/2024 | |
| 10.16# | License Agreement, by and between the Registrant and Sanofi, dated as of May 18, 2021 | S-1 | 333-276495 | 10.11 | 1/12/2024 | |

| Exhibit No. | Description | Form | File No. | Exhibit | Filing Date | Filed Herewith |
|---|---|---|---|---|---|---|
| 10.17# | Patent and Know-How License Agreement, by and between the Registrant and Cerecor Inc. (k/n/a Avalo Therapeutics, Inc.), dated as of May 28, 2021 | S-1 | 333-276495 | 10.12 | 1/12/2024 | |
| 10.18# | Exclusive License Agreement, by and between Dow Agrosciences LLC and Neuralstem, Inc., dated as of December 1, 2016. | S-1 | 333-276495 | 10.13 | 1/12/2024 | |
| 10.19† | Asset Transfer Agreement, by and between the Registrant and Palisade Bio, Inc. (formerly Seneca Biopharma, Inc., formerly Neuralstem Inc.), dated as of October 18, 2021 | S-1 | 333-276495 | 10.14 | 1/12/2024 | |
| 10.20 | Assignment and Assumption Agreement, by and between the Registrant and Palisade Bio, Inc. (formerly Seneca Biopharma, Inc., formerly Neuralstem Inc.), dated as of October 18, 2021 | S-1 | 333-276495 | 10.15 | 1/12/2024 | |
| 10.21# | Asset Purchase Agreement, by and between the Registrant and Teva Pharmaceutical Industries, Ltd., dated as of October 4, 2021 | S-1 | 333-276495 | 10.16 | 1/12/2024 | |
| 10.22# | Joint Development and License Agreement, by and between the Registrant and MedRx Co., Ltd., dated as of September 25, 2023 | S-1 | 333-276495 | 10.17 | 1/12/2024 | |
| 10.23† | Convertible Loan Agreement, by and between the Registrant and The Wellcome Trust Limited, dated as of July 24, 2024 | 8-K | 001-41944 | 10.1 | 7/29/2024 | |
| 19.1 | Insider Trading Policy | | | | | X |
| 21.1 | Subsidiaries of the Registrant | | | | | X |
| 23.1 | Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm | | | | | X |
| 31.1 | Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | | | | | X |

| Exhibit No. | Description | Form | File No. | Exhibit | Filing Date | Filed Herewith |
|---|---|---|---|---|---|---|
| 31.2 | Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | | | | | X |
| 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 | | | | | X |
| 32.2* | Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 | | | | | X |
| 97 | Incentive Compensation Recoupment Policy | 10-K | 001-41944 | 97 | 3/21/2024 | |
| 101.INS | Inline XBRL Instance Document | | | | | X |
| 101.SCH | Taxonomy Extension Schema with Embedded Linkbase Documents | | | | | X |
| 104 | Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibits 101) | | | | | X |

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+ Indicates management contract or compensatory plan.

† Certain schedules and exhibits to this exhibit have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the SEC upon request.

# Pursuant to Item 601(b)(10) of Regulation S-K, portions of this exhibit have been omitted as the registrant has determined that the omitted information is (i) not material and (ii) the type of information that the registrant customarily and actually treats as private or confidential.

* This certification is deemed not filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

**Item 16. Form 10-K Summary.**

None.

## SIGNATURES

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

**ALTO NEUROSCIENCE, INC.**

Date: March 20, 2025

By: /s/ Amit Etkin
Amit Etkin, M.D., Ph.D.
President and Chief Executive Officer

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

| Signature | Title | Date |
|---|---|---|
| /s/ Amit Etkin<br>Amit Etkin, M.D., Ph.D. | President, Chief Executive Officer, and Chair of the Board of Directors<br>*(Principal Executive Officer)* | March 20, 2025 |
| /s/ Nicholas Smith<br>Nicholas Smith | Chief Financial Officer and Chief Business Officer<br>*(Principal Financial Officer and Principal Accounting Officer)* | March 20, 2025 |
| /s/ Po Yu (Jeff) Chen<br>Po Yu (Jeff) Chen, Ph.D. | Director | March 20, 2025 |
| /s/ Christopher Nixon Cox<br>Christopher Nixon Cox | Director | March 20, 2025 |
| /s/ Andrew Dreyfus<br>Andrew Dreyfus | Director | March 20, 2025 |
| /s/ Husseini Manji<br>Husseini Manji, M.D. | Director | March 20, 2025 |
| /s/ Maha Radhakrishnan<br>Maha Radhakrishnan, M.D. | Director | March 20, 2025 |
| /s/ Gwill York<br>Gwill York | Director | March 20, 2025 |

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ALTO NEUROSCIENCE

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