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 001-42121

Rapport Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**88-0724208**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. employer identification no.)**
1325 Boylston Street, Suite 401 Boston, MA	**02215**
(Address of principal executive offices)	**(Zip code)**

Registrant's telephone number, including area code: (857) 321-8020

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

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

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on the Nasdaq Global Market on June 28, 2024 was $474,516,072.

The number of shares of registrant's common stock outstanding as of March 1, 2025 was 36,496,437.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2025 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the end of the registrant's fiscal year ended December 31, 2024 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, results of preclinical studies, clinical trials, research and development costs, regulatory approvals, commercial strategy, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties, and other important factors that are in some cases beyond our control and 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.

In some cases, forward-looking statements can be identified by terms such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "believe," "estimate," "predict," "potential," or "continue" or the negative of these terms or other similar expressions. Forward-looking statements contained in this Annual Report may include, but are not limited to, statements about:

- our ability to identify, develop, and commercialize current and future product candidates based on our RAP technology platform;
- the initiation, timing, progress, and results of our research and development programs, preclinical studies and clinical trials, including our ability to resolve the U.S. Food and Drug Administration's clinical hold on our Phase 2a proof-of-concept trial of RAP-219 for the treatment of diabetic peripheral neuropathic pain;
- the translation of endpoints in our current and planned clinical trials to future registrational trials;
- our ability to replicate positive results from earlier preclinical studies or clinical trials conducted by us or third parties in current or future clinical trials;
- our ability to demonstrate that our current and future product candidates are safe and effective for their proposed indications;
- the number of patients with the diseases or disorders we elect to pursue with our product candidates, and the willingness of those patient populations to use and adhere to our product candidates if approved in the future;
- the implementation of our business model, and strategic plans for our business, programs, future product candidates, platform, and technology;
- our ability to advance any product candidates through applicable regulatory approval processes;
- our ability to obtain additional cash and the sufficiency of our existing cash, cash equivalents and short-term investments to fund our future operating expenses and capital expenditure requirements;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing;
- our ability to comply with our obligations under our intellectual property licenses with third parties, including Janssen Pharmaceutical NV;
- our ability to maintain, expand and protect our intellectual property portfolio;
- developments relating to our competitors and our industry;
- existing regulations and regulatory developments in the United States and other jurisdictions;
- our ability to identify and enter into future license agreements and collaborations;
- general economic, industry, and market conditions, including rising interest rates and inflation;
- our ability to attract, hire, and retain our key personnel and additional qualified personnel; and
- our anticipated use of our existing cash, cash equivalents and short-term investments.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this Annual Report. 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 the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events or otherwise.

You should read this Annual Report, the documents that we reference in this Annual Report and the other documents that we file with the Securities and Exchange Commission ("SEC") with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, which include, but are not limited to, the following:

•We are a clinical-stage biotechnology company with a limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability. We have incurred significant financial losses since our inception and anticipate that we will continue to incur significant financial losses for the foreseeable future.

•We will require additional funding in order to finance operations. If we are unable to raise capital when needed, or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

•Our business is highly dependent on the success of our product candidates, particularly RAP-219 for focal epilepsy. If we are unable to successfully complete clinical development, obtain regulatory approval for or commercialize one or more of our product candidates, or if we experience delays in doing so, our business will be materially harmed.

•The successful development of pharmaceutical products involves a lengthy and expensive process and is highly uncertain.

•Due to the significant resources required for the development of our pipeline, and depending on our ability to access capital, we must prioritize the development of certain product candidates over others. Moreover, we may fail to expend our limited resources on product candidates or indications that may have been more profitable or for which there is a greater likelihood of success.

•The regulatory approval processes of the Food and Drug Administration ("FDA"), European Medicines Agency ("EMA"), Medicines and Healthcare products Regulatory Agency ("MHRA") and other comparable regulatory authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

•We are dependent on a third party having accurately generated, collected, interpreted and reported data from certain preclinical studies and clinical trials that were previously conducted for our product candidates.

•If our clinical trials fail to replicate positive results from earlier preclinical studies or clinical trials conducted by us or third parties, we may be unable to successfully develop, obtain regulatory approval for or commercialize our product candidates.

•If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the development and commercialization of our product candidates may be delayed, and our business and results of operations may be harmed.

•Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if obtained.

•We have concentrated our research and development efforts on the treatment of disorders of the nervous system, a field that faces certain challenges in drug development.

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

•The number of patients with the diseases and disorders for which we are developing our product candidates has not been established with precision. If the actual number of patients with the diseases or disorders we elect to pursue with our product candidates is smaller than we anticipate, we may have difficulties in enrolling patients in our clinical trials, which may delay or prevent development of our product candidates. Even if such product candidates are successfully developed and approved, the markets for our product candidates may be smaller than we expect and our revenue potential and ability to achieve profitability may be materially adversely affected.

•We rely on third parties to assist in conducting our clinical trials. If they do not perform satisfactorily, we may not be able to obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

•We depend on in-licensed intellectual property. If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

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

The summary risk factors described above should be read together with the text of the full risk factors in the section titled "Risk Factors" and the other information set forth in this Annual Report, as well as in other documents that we file with the SEC. The risks summarized above or described in full elsewhere in this Annual Report are not the only risks that we face. Additional risks and uncertainties not presently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations, and future, growth prospects.

PART I

Item 1. Business

Overview

We are a clinical-stage biotechnology company dedicated to discovering and developing small molecule precision medicines for patients with neurological or psychiatric disorders. Our foundational science has elucidated complexities of neuronal receptor biology and enables us to map and target certain neuronal receptor complexes. Neuronal receptors are complex assemblies of proteins, comprising receptor principal subunits and their receptor associated proteins ("RAPs"), the latter of which play crucial roles in regulating receptor expression and function. We believe that our deep expertise in RAP biology provides an opportunity for us to interrogate previously inaccessible targets and develop neurological and psychiatric drugs that are specific for receptor variants and neuroanatomical regions associated with certain diseases. Most neuroactive drugs lack this specificity, often resulting in undesired and intolerable side effects. Leveraging our expertise, we are developing a portfolio of precision product candidates that we believe has the potential to transform the standard of care of many neurological and psychiatric disorders.

Our founders have made pioneering discoveries related to the function of RAPs in the brain. Their findings form the basis of our RAP technology platform, which enables a differentiated approach to generate precision small molecule product candidates with the potential to overcome many limitations of conventional neurology drug discovery. RAP-219, our most advanced product candidate, is an AMPA receptor ("AMPAR") negative allosteric modulator ("NAM"). RAP-219 is designed to achieve neuroanatomical specificity through its selective targeting of a RAP known as TARPγ8, which is associated with the neuronal AMPARs. Whereas AMPARs are distributed widely in the central nervous system ("CNS"), TARPγ8 is expressed only in discrete regions, including the hippocampus and neocortex, where focal seizures often originate. By contrast, TARPγ8 has minimal expression in the hindbrain, where drug effects are often associated with adverse events. As such, we believe RAP-219 has the potential for a differentiated profile as compared to traditional neuroscience medications. Due to the role of AMPA biology in various neurological disorders and our precision approach of selectively targeting TARPγ8, we believe RAP-219 has pipeline-in-a-product potential and we are evaluating it as a potentially transformational treatment for patients with focal epilepsy, bipolar disorder, and peripheral neuropathic pain.

A total of four Phase 1 trials in RAP-219 have been conducted to date in healthy adult volunteers: a single ascending dose ("SAD") trial; a multiple ascending dose ("MAD") trial; a second MAD trial ("MAD-2"), to assess dosing regimens that may accelerate time to reach therapeutic exposure; and a human positron emission tomography ("PET") trial, which utilized a companion PET radiotracer to confirm brain target receptor occupancy and brain region specificity across a range of dosing and exposure levels. In January 2025, we announced results from our PET and MAD-2 trials of RAP-219. Data demonstrated that neuroanatomical specificity can be achieved through RAP-219's selective targeting of TARPγ8. In Cohort 1 of the human PET trial, which used the dosing regimen utilized in our ongoing Phase 2a trial in patients with refractory focal epilepsy, RAP-219 achieved target receptor occupancy associated with maximal seizure protection in preclinical models within five days and was generally well tolerated, which we believe further supports the use of such dosing regimen in the Phase 2a trial.

We are currently conducting a Phase 2a proof-of-concept trial in adult patients with refractory focal epilepsy, for which we expect to report topline results in the third quarter of 2025. We believe RAP-219 also has therapeutic potential in bipolar disorder and peripheral neuropathic pain, and we intend to initiate a Phase 2a proof-of-concept trial in bipolar mania in the third quarter of 2025 with topline results expected in the first half of 2027. We were notified in the fourth quarter of 2024 by the U.S. Food and Drug Administration ("FDA") that the Investigational New Drug ("IND") submitted for the initiation of a Phase 2a proof-of-concept trial of RAP-219 for the treatment of diabetic peripheral neuropathic pain ("DPNP") was placed on clinical hold. The FDA requested additional information and amendments specific to the protocol design. The clinical hold is specific to the IND for DPNP and has not impacted our ongoing Phase 2a trial in refractory focal epilepsy or planned proof-of-concept trial in bipolar mania. We believe in our ability to advance the clinical development of RAP-219 for DPNP and will provide an update on the anticipated timing of the Phase 2a trial initiation once available.

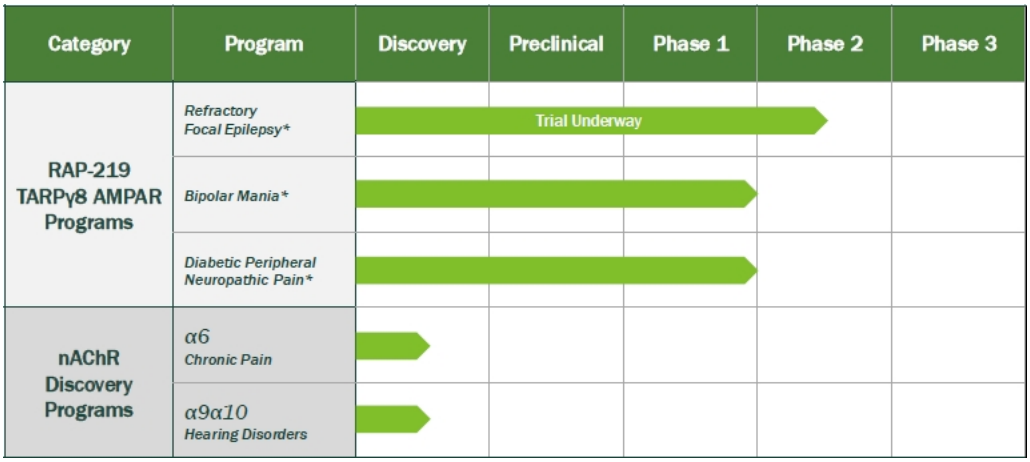
We have also identified another TARPγ8 targeted molecule with differentiated chemical and pharmacokinetic properties, RAP-199. However, with growing confidence in RAP-219 and a commitment to disciplined capital allocation, we are deferring further investment in RAP-199 and focusing our resources on execution of our three RAP-219 proof-of-concept clinical trials.

Beyond TARPγ8, we have two advanced discovery-stage nicotinic acetylcholine receptor ("nAChR") programs stemming from our RAP technology platform. The first comprises modulators of α6 nAChRs that we are developing in chronic pain; and the second comprises modulators of α9α10 nAChRs that we are developing in hearing disorders. Third-party genetic data suggest that these nAChR subtypes could be attractive drug targets for these diseases. We continue to leverage our RAP technology platform to

discover additional product candidates that we believe have the potential to provide a transformative benefit for large patient populations with neurological or psychiatric diseases with unmet needs.

Our Pipeline

Our current portfolio of programs from our RAP technology platform is summarized in the pipeline chart below:



* We have conducted four Phase 1 trials in healthy adult volunteers supportive of multiple RAP-219 indications.

Introduction to RAP-219

RAP-219 is an investigational small molecule that is designed to inhibit TARPγ8-containing AMPARs with picomolar ("pM") affinity, which implies tight binding. Given RAP-219's mechanism of action, neuroanatomical specificity and target potency observed to date in preclinical studies, we believe it has the potential to be a differentiated therapy for focal epilepsy and other neurological and psychiatric disorders, including bipolar disorder and peripheral neuropathic pain.

Epilepsy is estimated to affect 50 million people worldwide, including approximately 3.0 million adults in the United States ("United States" or "U.S."). In 2022, the total branded market for epilepsy was approximately $2.8 billion, and this is expected to grow to approximately $3.6 billion by 2028. There are an estimated 1.8 million people in the United States who suffer from focal epilepsy, accounting for approximately 60 percent of patients with epilepsy. Focal epilepsy is characterized by seizures caused by intermittent abnormal electrical activity originating in specific areas of the brain. The hippocampus, located within the temporal lobe, is commonly associated with focal epilepsy, with approximately 50 percent of all seizures originating in or around this area. The cerebral cortex is another common site of focal onset seizure initiation, originating up to 50 percent of all seizures. However, the hippocampus often plays a role in these seizures as well, with the abnormal electrical brain activity that arises in the cerebral cortex often traveling to and being perpetuated by the hippocampus.

Epilepsy has profound negative impacts on a patient's quality of life, including limitations on social engagement, physical activity and independence. Recent studies have also found that epilepsy can result in cognitive impairment. The treatment goal for all patients with epilepsy, including focal epilepsy, is complete freedom from seizures. Despite there being more than 20 antiseizure medications ("ASMs") approved by the FDA, 30 to 40 percent of patients with epilepsy continue to experience recurring seizures despite taking two or more ASMs. This is termed "refractory epilepsy." In addition to providing sub-optimal efficacy, ASMs are commonly associated with risks of intolerable and debilitating adverse events ("AEs"). These side effects, such as cognitive impairment, sedation, ataxia and dizziness, are believed to result from drug actions in brain regions unrelated to epilepsy. These AEs often lead to dosing adjustments and patient nonadherence, both of which can limit efficacy. We believe tolerability, adherence and clinical benefit can be improved with RAP-219, an investigational therapy that is designed to precisely modulate only diseased brain regions.

Patients with epilepsy commonly take ASM combinations, which is referred to as polypharmacy. Drug-drug interactions make polypharmacy complex and add a further challenge to managing persistent seizures in epilepsy. When a physician adds a drug to a patient's regimen, they typically prioritize one with a differentiated mechanism of action, an approach referred to as rational

polypharmacy. Therefore, there is a critical need for therapies with new mechanisms of action, fewer AEs and a mitigated risk of drug-drug interaction for the treatment of focal epilepsy.

AMPAR inhibition is a clinically validated approach in treating epilepsy, with perampanel (marketed as FYCOMPA) approved by the FDA in 2012 for both focal and generalized epilepsy. Whereas perampanel binds to AMPARs throughout the CNS and periphery, RAP-219's actions on AMPARs are restricted to those few specific regions where TARPγ8 is expressed, most notably the hippocampus. This leads us to believe that the tolerability profile of RAP-219 could be significantly differentiated from that of perampanel and other currently available ASMs.

TARPγ8 is expressed in specific brain regions, being most enriched in the hippocampus and other forebrain structures that are key sites associated with focal onset seizures. As brain regions with TAPRγ8 expression closely overlay with the brain sites most often involved with the pathophysiology of focal epilepsy, we believe that RAP-219 has potential to provide a differentiated profile. Furthermore, TARPγ8 expression is enriched in the hippocampus, amygdala, and cerebral cortex and has minimal expression in certain other areas that are critical for normal brain functions, including the cerebellum and brainstem. In contrast to the precision mechanism of RAP-219, the majority of ASMs, including perampanel, bind their target receptors throughout the brain, and we believe this lack of anatomical specificity may contribute to their side effect profiles. We believe that RAP-219, as compared to currently available ASMs, has the potential to have a greater therapeutic index, meaning a wider range of doses at which it is likely to be effective without causing unacceptable AEs. If RAP-219 is approved, this could have important clinical utility for the management of focal epilepsy.

We observed RAP-219 to be generally well tolerated in the four phase 1 trials evaluating RAP-219 in healthy adult volunteers we have conducted to date. The plasma concentrations of RAP-219 measured during those trials suggested that once-daily oral administration with a simple dosing schedule could achieve our targeted therapeutic exposures (3 ng/mL to 7 ng/mL). For our ongoing Phase 2a proof-of-concept trial, we are enrolling adult patients with refractory focal epilepsy who have an implanted responsive neurostimulation ("RNS") system, an FDA approved device for refractory focal onset epilepsy. The RNS system includes an electrode that continually monitors intracranial brain waves and detects the magnitude, duration and frequency of spectrographic activity, which are recorded as intracranial electroencephalography ("iEEG") data. We are using these iEEG data as the biomarker-based primary endpoint in our proof-of-concept trial. We believe these data could be translatable to a clinical seizure endpoint in future registrational trials. We expect to release topline results from this Phase 2a proof-of-concept trial in refractory focal epilepsy in the third quarter of 2025.

Introduction to Our Discovery-Stage Nicotinic Acetylcholine Receptor Programs

In addition to RAP-219, we have two discovery-stage programs stemming from our RAP technology platform. Our α6 nAChR and α9α10 nAChR programs were both enabled by our discovery of RAPs that drive the assembly of functional versions of these receptors in cell lines. Based on third-party genetic data, we believe each of these nAChR subtypes could be attractive drug targets. However, it was not until our identification of these RAPs that it became possible to create cell lines for *in vitro* compound screening and optimization against these important targets.

We are pursuing agonists and positive allosteric modulators ("PAMs") of the α6 nAChR in chronic pain. Gain-of-function variants in the gene encoding the α6 subunit can attenuate pain levels. A previous third-party investigational pan-nAChR agonist demonstrated clinical activity in a randomized placebo controlled study in painful diabetic neuropathy but this experimental therapeutic was associated with intolerable side effects, which led to the discontinuation of its development. We believe that these side effects were primarily due to the non-selective nature of that agonist. Through our ability to functionally express and pharmacologically screen for α6 nAChR modulators, we have identified small molecule agonists and PAMs that showed α6 nAChR selectivity as well as beneficial activity in a preclinical model of peripheral neuropathic pain. We are optimizing these molecules in anticipation of selecting candidates to advance into the clinic.

Our α9α10 nAChR program focuses on the discovery of small molecule modulators of this receptor as potential therapies for hearing disorders. Third-party studies observed a loss-of-function mutation of the gene for the α9 subunit in mice associated with increased sensitivity to noise-induced hearing loss. Conversely, we observed a gain-in-function mutation in α9 protected against hearing loss. We have identified small molecule modulators of α9α10 nAChR and are now optimizing these molecules in anticipation of selecting candidates to advance into the clinic.

Our Company's History and Our Team

Rapport was formed in February 2022, with founding support from Third Rock Ventures and Johnson & Johnson Innovation-JJDC, to advance the discovery and development of RAP-targeted precision neuromedicines. Our scientific founder and Chief

Scientific Officer, David Bredt, M.D., Ph.D., pioneered the discovery of RAPs and their targeting by small molecules at Janssen Pharmaceutical NV ("Janssen").

In August 2022, we entered into a license agreement with Janssen (the "Janssen License") for the research, development and commercialization of certain TARPγ8 products, including RAP-219 and nAChR projects created by Dr. Bredt and his colleagues at Janssen. We are furthering development of these assets and extending discovery efforts into novel areas. Under the terms of the Janssen License, certain TARPγ8 and nAChR patents, materials and know-how were transferred to us. All discovery and development efforts related to our pipeline programs are herein referred to as "ours," although some of these preclinical efforts were completed at Janssen prior to the Janssen License. In many cases, these efforts were made by certain of the same personnel who have since joined Rapport.

In addition to Dr. Bredt, we have a seasoned leadership team with deep expertise in building novel therapeutic platforms, bringing therapeutics to market and supporting the growth of public biopharmaceutical and biotechnology companies, such as Abraham N. Ceesay, M.B.A., our Chief Executive Officer and a member of our board of directors, Troy Ignelzi, our Chief Financial Officer, Jeffrey Sevigny, M.D., our Chief Medical Officer, Cheryl Gault, our Chief Operating Officer, Swamy Yeleswaram, Ph.D., our Chief Development Officer, Kathy Wilkinson, our Chief People Officer and Karina Chmielewski, our Chief Information Officer.

Our Strategy

Leveraging our RAP technology platform, we strive to become a leader in precision neuroscience through the discovery and development of transformational small molecule medicines for patients with neurological or psychiatric disorders. As key elements of our strategy, we intend to:

- **Advance RAP-219 clinical development in focal epilepsy.** RAP-219 is designed as a highly potent and selective NAM of TARPγ8-AMPAR which has demonstrated antiseizure activity in preclinical epilepsy models without evidence of motoric impairment or sedation characteristic of many approved ASMs.
- **Expand the potential of RAP-219 in additional neurological and psychiatric indications**. We believe that RAP-219's ability to precisely modulate the activity of AMPARs within specific CNS regions, provides the potential for clinical applications in neurological indications beyond focal epilepsy.
- **Extend the life cycle of RAP-219 and expand the TARPγ8 franchise.** We are exploring a long- acting injectable formulation of RAP-219, which we believe will expand the potential clinical utility across RAP-219's indications and potentially extend the molecule's lifecycle.
- **Advance development of our RAP-enabled nAChR programs.** Our RAP platform has enabled identification of small molecules specific for nAChR drug targets we find compelling. We believe that our α6 nAChR program may deliver clinical benefits in chronic pain while avoiding the AEs associated with non-selective nAChR agonists. We believe that compounds specific to the α9α10 receptor could provide therapeutic benefit in hearing disorders. We are optimizing molecules for both programs, in anticipation of selecting lead candidates to advance into the clinic.
- **Fortify our leadership position in RAP-enabled drug discovery to expand our pipeline of transformative precision neuroscience therapies for patients.** We believe the science underpinning our RAP technology platform can serve as the foundation for a broad portfolio of precision neuroscience product candidates that have the potential to transform the current treatment armamentarium for many neurological and psychiatric disorders. We are committed to leveraging our expertise in RAP biology to develop a portfolio of small molecule therapies to deliver potentially more effective, better tolerated and safer treatments to large and underserved neurological and psychiatric patient populations.
- **Pursue strategic partnerships opportunistically**. We currently have exclusive global rights to use our technology platform and to commercialize our product candidates. If we believe that partnerships can accelerate the development or maximize the market potential of our product candidates, we will consider entering into product, target and/or geographic specific strategic partnerships on an opportunistic basis.

Our RAP Technology Platform

Our founders are pioneers of RAP biology who have made key discoveries related to RAP function. Their findings form the basis of our RAP technology platform, which can potentially provide a differentiated approach to generate precision small molecule product candidates.

Due to the complexities of studying drug activity in the brain, a standard approach to discovery and optimization of neurology drugs is through *in vitro* cellular assays involving recombinant receptors. This approach often fails to replicate the function of

relevant targets in their natural contexts and has resulted in the approval of neurology drugs that are not designed to be selective for specific forms of their targets, which can contribute to unwanted toxicities and limit therapeutic indexes.

We believe that leveraging RAPs can overcome many limitations of conventional neurology drug discovery. RAPs have defining characteristics that we believe make them ideal tools in the development of precision neuromedicines. First, because RAPs play critical roles in modulating receptor assembly and function, understanding RAP biology provides powerful insights into neuronal signaling. Second, because RAPs can be differentially expressed in specific brain regions, we believe they can serve as drug targets with neuroanatomical specificity.

Using two distinct strategies, we are leveraging our expertise in RAP biology to develop a portfolio of precision neuroscience product candidates that we believe will transform the treatment of many neurological and psychiatric disorders. One strategy uses a RAP as a direct target, which can be more precise than drugging a receptor itself. RAP-219 exemplifies this, as it has been shown in preclinical studies to bind to an AMPA RAP, TARPγ8, which is enriched in brain regions that initiate or perpetuate seizures in focal epilepsy.

A second strategy uses RAPs to "unlock" receptors for potentially first-in-class drug discovery programs. Many receptors cannot function without their RAPs, and such receptors have therefore been inaccessible to study *in vitro*. Our discovery platform integrates cutting-edge genetics with functional proteomics to discover RAPs that are regionally localized and involved in disease-related signaling. We have designed our platform to prosecute a wide range of validated therapeutic targets. This second strategy enabled our discovery stage nAChR programs, which focus on α6 and α9α10.

RAP-219, Our TARPγ8 Specific Product Candidate

Ionotropic receptors for glutamate ("iGluR") are ligand gated ion channels activated by the neurotransmitter glutamate. These receptors mediate most excitatory synaptic transmission throughout the CNS. iGluRs comprise four subtypes based on their ligand binding properties: AMPARs, kainate receptors, N-methyl-D-aspartate ("NMDA") receptors and delta receptors. The glutamate signaling pathway is targeted by FDA approved drugs for indications such as epilepsy, schizophrenia, Alzheimer's disease and Parkinson's disease. However, these medicines are associated with numerous side effects, such as sedation, ataxia, cognitive impairment and neuropsychiatric symptoms. These undesired effects may be exacerbated by the impact of these drugs on glutamate receptors throughout the brain.

AMPARs are cation, or positively charged ion, channels that open to permit the influx of sodium ions (Na+) to depolarize postsynaptic membranes. Our lead asset, RAP-219, is an investigational small molecule designed to potently and specifically inhibit TARPγ8-containing AMPARs. Because TARPγ8 expression is restricted to specific brain regions such as the hippocampus, which are often involved in focal epilepsies, we believe RAP-219 has the potential to provide a differentiated clinical profile, including improved activity and tolerability. In preclinical epilepsy models, RAP-219 reduced seizures without inducing sedation or motoric impairment, which are side effects that plague most existing ASMs. Owing to pharmacology studies in animal models as well as expression of TARPγ8 in spinal cord and limbic system, we believe RAP-219 may treat bipolar disorder and peripheral neuropathic pain. The initial formulation of RAP-219 is planned to be a once-per-day oral tablet. We are also developing a long-acting injectable formulation for once a month or even less frequent dosing, which we believe will result in better compliance and patient outcomes.

Background to Focal Epilepsy

Epilepsy is a chronic neurological disorder characterized by spontaneous recurrence of sudden abnormal bursts of brain electrical activity that disrupt brain function and cause seizures. Epilepsy is estimated to affect 50 million people worldwide including 3.0 million adults in the United States. Epilepsy is the third most common neurological disorder, with almost 10 percent of people experiencing a seizure during their lives. The annual direct costs, including outpatient, inpatient, emergency care and treatment costs, of epilepsy in the United States are estimated to be $28 billion.

Epilepsy can be divided into subgroups defined by the types of seizures that occur:

•Generalized epilepsy is characterized by seizures affecting broad areas of the brain. The most severe type is known as tonic-clonic seizures, which involve sudden loss of consciousness, body stiffening, twitching and shaking. In other cases, these patients can experience subsets of these symptoms. Generalized seizures account for 40 percent of all epilepsies.

•Focal epilepsy is characterized by seizures affecting more restricted areas of the brain. Focal epilepsy, which sometimes results in loss of consciousness or awareness, can lead to changes in the way things look, smell, feel, taste or sound. These seizures may be accompanied by involuntary jerking of a body part or by repetitive movements such as hand

rubbing, chewing, or swallowing. Focal epilepsies account for 60 percent of all epilepsies. Figure 1 below illustrates the prevalence of focal epilepsy in the United States.

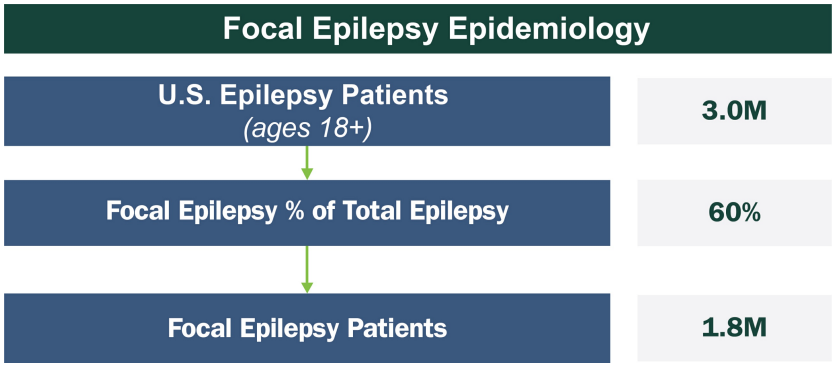


Figure 1. The prevalence of focal epilepsy in the United States is estimated to be 1.8 million patients.

The unpredictable nature of epilepsy has a profound negative impact on patient quality of life. Patients often limit their social engagement and physical activity for fear of seizures. Epilepsy also limits patients' ability to function independently. For instance, in some U.S. states, individuals with epilepsy are required to have a record of being seizure-free for 3 to 12 months in order to drive. Epilepsy is often associated with depression, anxiety and psychosis and doubles the incidence of mental health disorders. Furthermore, epilepsy also presents serious mortality risk with approximately one percent of patients suffering sudden unexpected death in epilepsy ("SUDEP"). Having uncontrolled seizures increases the risk of SUDEP. Both treatment and indirect costs for individuals with uncontrolled epilepsy are significantly higher than for those with stable epilepsy.

Current Standard of Care and Limitations

Treatment strategies for focal epilepsy can include both medical and surgical options, which strive to achieve seizure control with minimal AEs. Although there are over 20 FDA approved ASMs, 30 to 40 percent of patients have refractory epilepsy and continue to experience uncontrolled seizures despite taking two or more ASMs. First-line treatment for focal epilepsy is monotherapy, prescribing one ASM which is selected based on a patient's seizure type, medical history and their physician's experience with a drug's efficacy, tolerability and convenience.

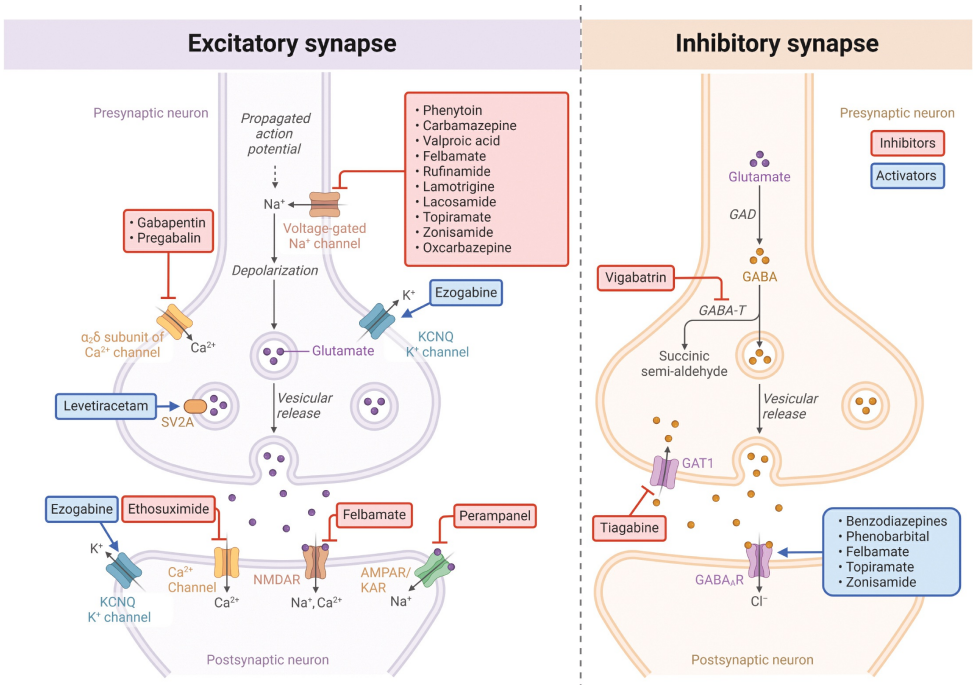
Approved ASMs have many mechanisms of action, and most work by either inhibiting neuronal excitation or augmenting neuronal inhibition. Some ASMs blunt excitation by inhibiting voltage sensitive sodium or calcium channels or by blocking excitatory AMPA or NMDA receptors. Alternatively, some ASMs augment inhibition by enhancing γ-aminobutyric acid type A ("$GABA_A$") receptors or voltage-gated potassium channels. In addition, there are some ASMs for which the precise mechanism of action is not known and some which engage multiple targets. Most ASMs bind to targets expressed throughout the brain, and we believe this broad pharmacology can drive their side effects.

If a single ASM fails to prevent seizures, physicians often prescribe a different ASM or begin polypharmacy. When a prescribing physician decides which ASM to add to a refractory patient's drug regimen, one important factor is the desire to add a new ASM with a different mechanism of action from those ASMs the patient is already taking. The process of polypharmacy involves trial and error which can elevate risk of AEs and drug-drug interactions. Tolerability issues can lead patients to take suboptimal doses to minimize side effects or can lead to treatment discontinuation, which occurs in 30 to 40 percent of patients. AEs commonly reported with ASMs include systemic effects such as nausea and vomiting, neurologic effects such as sedation, cognitive effects, ataxia and dizziness. In addition, some ASMs are associated with severe medical safety risks, for example, rare idiosyncratic reactions such as the life- threatening multi-organ hypersensitivity reaction known as Drug Rash with Eosinophilia and Systemic Symptoms (DRESS), serious skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis, bone marrow suppression, significant liver and kidney abnormalities, and cardiac arrhythmias.

Antiseizure Therapy Through Modulation of Glutamate Signaling

Glutamate is the major excitatory neurotransmitter in the brain. Glutamate releases from presynaptic nerve terminals and the activation of postsynaptic receptors are critical for neurotransmission. Correspondingly, processes associated with glutamate release and its downstream signaling are highly regulated. Elevation in extracellular glutamate levels can lead to seizures, and many ASMs target this pathway.

ASMs can blunt glutamate-dependent signaling through diverse mechanisms. Drugs such as phenytoin, carbamazepine, lamotrigine and lacosamide molecule voltage-gated sodium channels and inhibit action potentials from reaching the glutamate release machinery within the presynaptic nerve terminal. Other drugs such as ethosuximide and ezogabine modulate voltage-gated calcium and potassium channels, respectively, which also can prevent the presynaptic release of glutamate. Figure 2 below shows the mechanisms of currently approved ASMs, including many that modulate glutamate signaling.



Source: Created with Biorender.com. Bialer M, White HS. (2010). Key factors in the discovery and development of new antiepileptic drugs. Nature Reviews Drug Discovery, 9(1):68–82. doi: 10.1038/nrd2997. Löscher W, Klein P. (2021). The Pharmacology and Clinical Efficacy of Antiseizure Medications: From Bromide Salts to Cenobamate and Beyond. CNS Drugs (2021) 35:935 -963. doi: 10.1007/s40263-021-00827- 8.

Figure 2. Mechanistic cartography of currently approved ASMs acting on the excitatory synapse (Left) and the inhibitor synapse (Right).

After being released into the synaptic cleft, glutamate can bind to AMPARs on postsynaptic neurons. This process permeates sodium and other cations, triggering a series of events that can ultimately lead to the generation of an action potential and the propagation of neuronal signals. Perampanel directly blocks the gating of all AMPARs, while other drugs, such as phenobarbital and tiagabine, oppose glutamate signaling by increasing the activity of inhibitory synaptic signaling driven by the $GABA_A$ receptors. Figure 2 above shows the mechanistic cartography of existing ASMs, including many that modulate glutamate signaling in the excitatory synapse.

Validation of AMPAR as a Target in Epilepsy

Perampanel, developed by Eisai Co. Ltd. and currently marketed as FYCOMPA by Catalyst Pharmaceuticals, Inc., is an FDA approved ASM that directly antagonizes all AMPARs throughout the brain. In three clinical trials of patients with refractory focal epilepsy, perampanel reduced the frequency of partial onset (focal) seizures by 31 to 34 percent compared to 10 to 21 percent in the placebo group. However, perampanel's efficacy was accompanied by frequent AEs consistent with its pan-AMPAR activity. At the highest recommended dose of perampanel (12 mg per day), over 40 percent of patients experienced dizziness, 18 percent reported somnolence, and at least 10 percent reported headaches, irritability, fatigue and falls. Perampanel's FDA approval label is accompanied by a black box warning for serious psychiatric and behavioral reactions, including aggression, hostility and homicidal ideation and threats. Furthermore, significant drug-drug interactions were reported for perampanel. The concomitant use with the other ASMs carbamazepine, phenytoin and oxcarbazepine decreased plasma levels of perampanel by approximately 50 to 67 percent. In addition, perampanel at a dose of 12 mg per day reduced exposure of levonorgestrel, an oral contraceptive, by approximately 40 percent.

We believe there are at least three critical differences between perampanel and RAP-219. First, their chemical structures are completely different. Second, perampanel and RAP-219 have entirely distinct binding sites. Whereas perampanel binds directly to AMPAR GluA subunits, RAP-219 is designed to interact with γ8, but not other TARP subtypes, and only when TARPγ8 is associated with GluA proteins. Third, whereas perampanel blocks AMPARs throughout the brain and body, RAP-219 activity on AMPARs has been observed to be restricted to those specific neurons that express TARPγ8, which are primarily located in the select forebrain regions. As such, we believe the tolerability profile of RAP-219 will be differentiated from that of perampanel, and may not induce the intolerable side effects associated with perampanel, such as dizziness, somnolence, fatigue, falls and vertigo.

Preclinical Studies Supportive of RAP-219

Preclinical studies have demonstrated RAP-219's pharmacology and pharmacodynamic properties, as summarized below. In addition, preclinical studies have been conducted with third-party and earlier generation TARPγ8 NAMs by us and third-parties, the results of which we believe are supportive of RAP-219 because these third-party and earlier generation TARPγ8 NAMs share the same binding site and have similar pharmacological effects as RAP-219.

TARPγ8 Expression is Localized

TARPγ8 is expressed in specific brain regions, being most enriched in the hippocampus, and also present in the amygdala and cortex. In a study completed by Janssen, radiolabeled TARPγ8 ligands, such as [3H]JNJ-56022486 (an earlier generation TARPγ8 NAM), were shown to bind selectively to regions of the mouse brain in a distribution that overlapped TARPγ8 protein expression. The highest density radioactive [3H]JNJ-56022486 binding occurred in the hippocampus, which is also the region where the majority of focal seizures originate and the brain region where focal seizures originating in the cortex often spread. Radioligand binding of [3H]JNJ-56022486 also occurred in other brain regions that contain TARPγ8, including the amygdala, cerebral cortex and striatum, which can also be involved in seizure initiation and propagation. Importantly, the spread of seizures from the hippocampus into the amygdala has been shown in a third-party study to increase the risk of SUDEP in patients.

Figure 3 below illustrates the enrichment of TARPγ8 in mouse hippocampus. The left image derives from the Allen Brain Atlas, a publicly available database of gene expression in the brain, and depicts in red high levels of TARPγ8 messenger ribonucleic acid detected by *in situ* hybridization. The right image depicts with yellow and orange high levels of [3H]JNJ-56022486 binding detected by autoradiography.

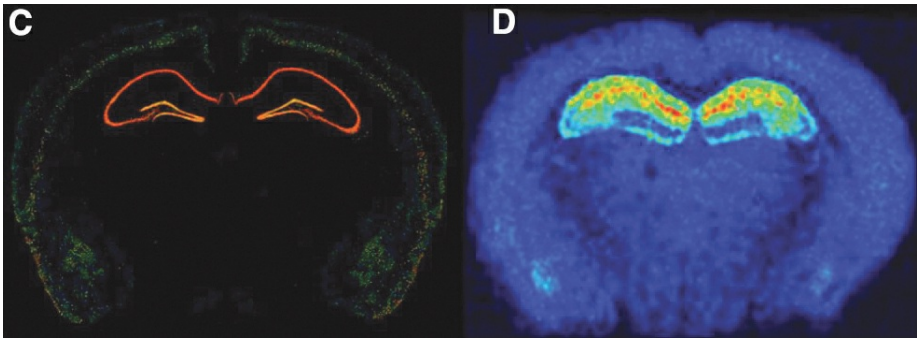


Figure 3. TARPγ8 is expressed in the mouse hippocampus.

TARPγ8 Ligands are Highly Selective Inhibitors of AMPAR

Structural analyses performed by a third party using cryogenic electron microscopy ("Cryo-EM") have shown that a TARPγ8 AMPAR NAM, JNJ-55511118 (an earlier generation TARPγ8 NAM), binds to an interface between TARPγ8 and AMPAR, which leads to alterations in the structure of the AMPAR, thereby negatively modulating receptor function and its ability to respond to glutamate. Third-party structural studies indicated that all TARPγ8 AMPAR NAMs tested bind in a similar mode, suggesting the potential for RAP-219 to also bind in this pocket between GluA and TARPγ8. Figure 4 illustrates TARPγ8 ligands binding to the interface between TARPγ8 and AMPAR.

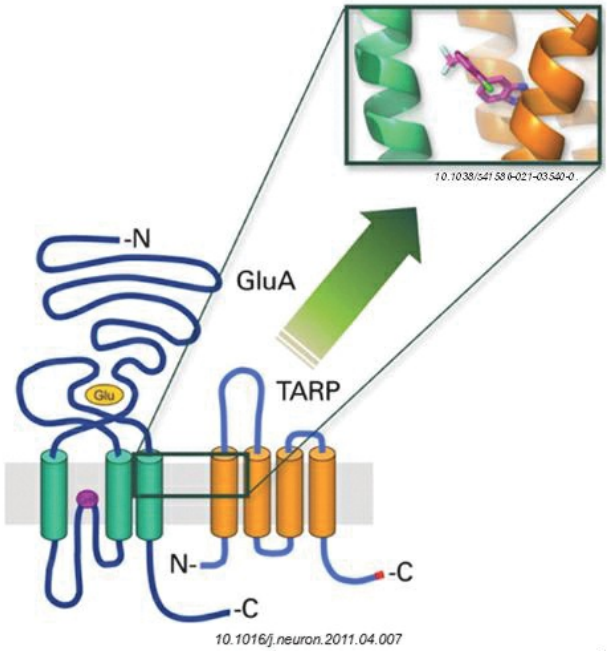


Figure 4. TARPγ8 ligands bind to the interface between TARPγ8 and AMPAR.

RAP-219 Was Observed to Be a Potent TARPγ8-Specific Inhibitor of AMPAR

Janssen tested RAP-219's effect on recombinant human GluA1-TARPγ8 complexes in mice and rats. The study found that RAP-219 inhibited the function of GluA1-TARPγ8 receptors with half maximal effect, referred to as the IC_{50}, at a concentration of approximately 100 pM, demonstrating RAP-219's potency. By contrast, as exemplified in Figure 5 below, RAP-219 was found to be far less potent on complexes of GluA1 with other relevant TARP isoforms, including γ2, γ3, γ4 or γ7 or on other receptor types, such as NMDA receptors, G protein-coupled receptors ("GPCRs"), enzymes or and kinases.

RAP-219 potency and selectivity	
TARPγ8-containing AMPA receptors (IC_{50})	**~100 pM**
vs. AMPA receptors (GluA1) lacking TARPs	>100,000x
vs. AMPA receptors containing other TARPs (γ2, γ3, γ4, γ7)	>4,000x
vs. NMDA receptors (2A, 2B, 2D)	>500,000x
vs. GPCRs/ion channels/enzymes (panel of 52)	>10,000x
vs. kinases (panel of 373)	>100,000x

Figure 5. RAP-219 observed to be a highly selective inhibitor of TARPγ8 AMPAR.

RAP-219 Was Observed to Be Bioavailable and CNS Penetrant in Animal Models

Oral doses of RAP-219 were rapidly absorbed with over 80 percent bioavailability in mice, rats, dogs and non-human primates. In these animal studies, completed by Janssen, RAP-219 had a half-life of 17.8 to 38.3 hours and was observed to distribute into the brain with a brain-to-plasma ratio of 0.96 in rats. Figure 6 below shows that oral doses of 0.02 mg/kg in the mouse and 0.01 mg/kg in the rat resulted in 50 percent TARPγ8- receptor/AMPAR occupancy for RAP-219 in the hippocampus, referred to as "ED_{50}."

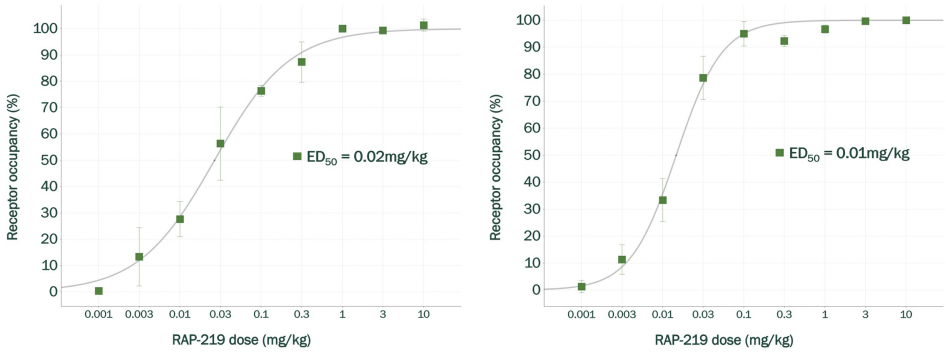


Figure 6. Dose dependent receptor occupancy of RAP-219. Following oral dosing of RAP-219, AMPAR occupancy was quantified in the hippocampus of the mouse (A) at 24 hours and rat (B) at 4 hours after dosing using ex-vivo autoradiography.

RAP-219 has the Potential for Reduced Drug-Drug Interactions Versus Approved ASMs

RAP-219 is neither a substrate nor an inhibitor of cytochrome P450 ("CYP") enzymes. CYPs comprise a large and diverse family of enzymes, responsible for the detoxification of many drugs, including ASMs. Drug- drug interactions with CYPs can decrease or increase ASM blood levels, which can reduce drug effectiveness or increase relevant drug side effects, respectively. RAP-219 has not been observed to induce or inhibit or be metabolized by any evaluated CYPs at clinically relevant concentrations. The systemic clearance of RAP-219 in humans appears to be predominantly via phase 2 conjugation. We believe that RAP-219's lack of interaction with the CYP pathway has the potential to reduce drug-drug interactions, which would serve as an advantage given the widespread use of polypharmacy in focal epilepsy, bipolar disorder and peripheral neuropathic pain.

RAP-219 Preclinical Trials in Focal Epilepsy

Multiple preclinical epilepsy models were used by Janssen to assess the potential of ASMs. In the pentylenetetrazol ("PTZ") infusion mouse model of acute seizures, RAP-219 administration was associated with an increased seizure threshold. PTZ is a $GABA_A$ receptor antagonist, which causes acute severe seizures in animals when infused at a high dose. As shown in Figure 7 below, RAP-219 led to a dose-dependent increase in the threshold concentration required to trigger both twitch and clonus in the Metrazol mouse model. Significant differences compared to vehicle treatment were detected in 0.1 and 1 mg/kg doses ($P<0.01$) for both twitch and clonus. ED_{50} values were 0.02 mg/kg for both twitch and clonus responses.

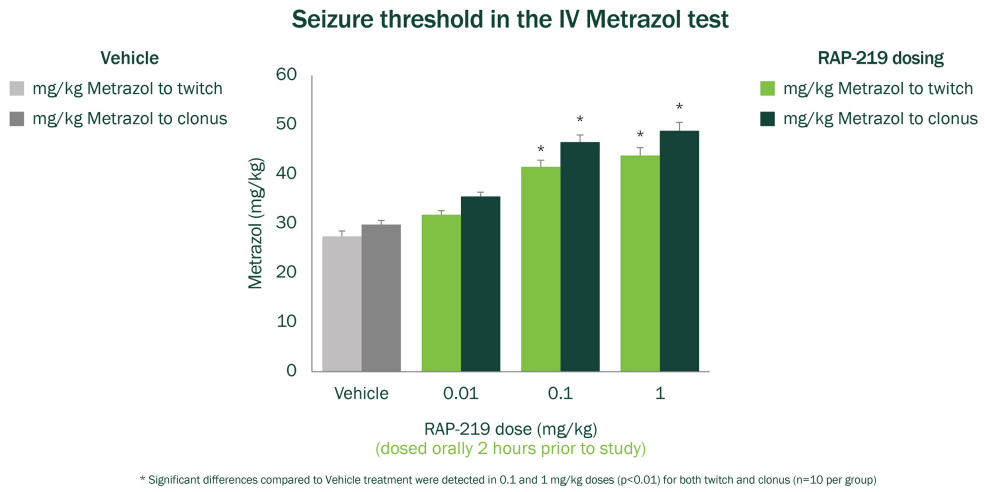


Figure 7. RAP-219 led to a dose dependent increase in the threshold concentration required to trigger both twitch and clonus responses in the IV Metrazol model.

The corneal kindling induced seizure model in mice is considered to be a valid model in focal epilepsy. In this model studied by Janssen, repeated application of an electrical stimulus, which is initially subconvulsive, resulted in alterations in brain function that led to progressive sensitization to seizures. As illustrated in Figure 8 below, in fully kindled mice, oral administration of a single dose of RAP-219 at doses of 0.02 mg/kg to 3 mg/kg prevented seizures with an estimated half maximal effective concentration ("EC50") occurring at 2.3 ng/mL plasma concentration. Immediately prior to the corneal kindling test, the same mice were assessed with a rotarod test. This is a performance test widely used to assess motor impairment and sedation in rodents. The lack of motoric

impairment with RAP-219, even at approximately 100-fold higher exposures, is consistent with the lack of expression of TARPγ8 in brain regions involved in motor coordination and sedation, such as the hindbrain.

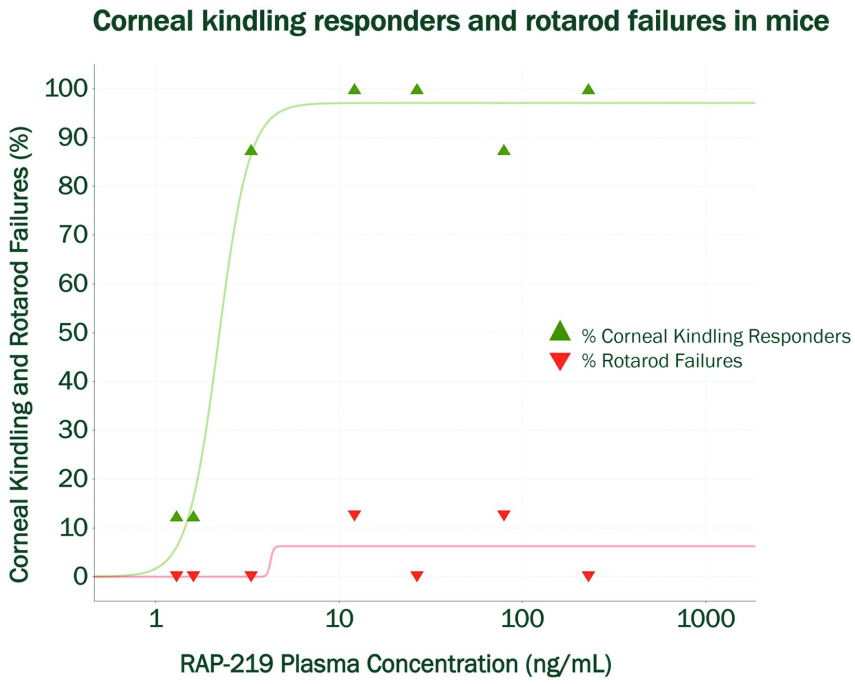


Figure 8. RAP-219 had an estimated EC50 of 2.3 ng/mL in the corneal kindling mouse model of focal epilepsy.

Maximal seizure protection, based on the percentage of responding animals, was observed at a plasma concentration of approximately 10 ng/mL, and significant seizure reduction was seen at a plasma concentration of approximately 7 ng/mL. This corresponds to a projected receptor occupancy of approximately 50 to 70 percent based on data generated in rats as measured by ex-vivo autoradiography, as shown in Figure 9 below.

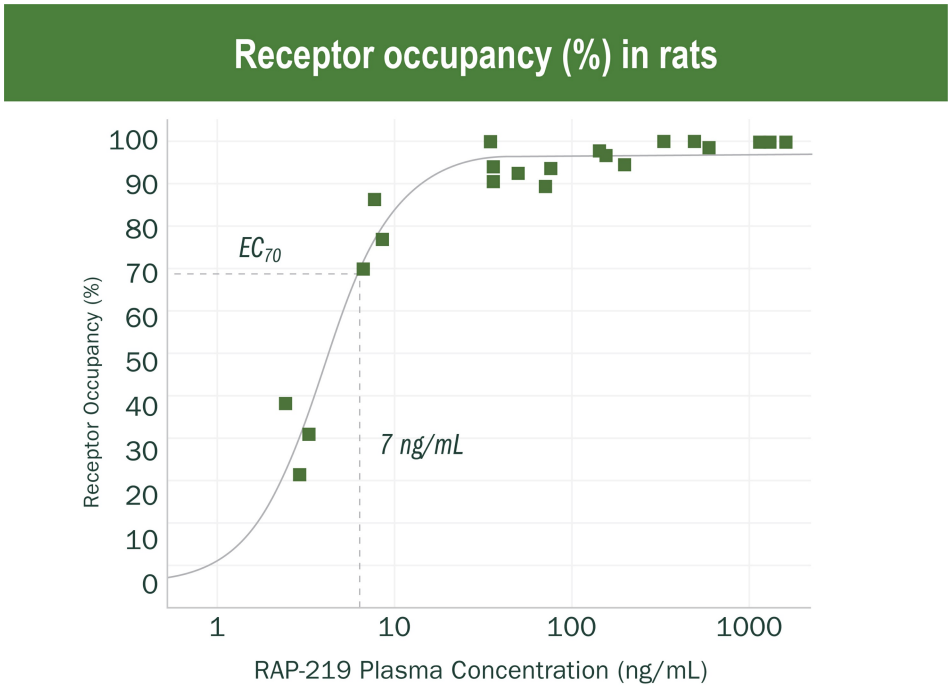


Figure 9. A plasma concentration of 7 ng/mL of RAP-219 corresponded to approximately a 70 percent receptor occupancy in rats.

Data from a separate study completed by us, in fully kindled mice, suggests that oral administration of RTX-1738 (a TARPγ8 NAM licensed to us under the same patent as RAP-219) at 3 mg/kg prevented seizures after either a single administration or after seven consecutive days of dosing, indicating that antiseizure activity was maintained with repeat dosing, i.e. no tolerance to the antiseizure activity was observed.

We believe that one potential advantage of the precision targeting observed with RAP-219 in preclinical models is a wide therapeutic index that may be achieved by avoiding AMPAR modulation in the hindbrain. The therapeutic index measures the general tolerability of a drug, reflecting the range of doses at which a medication is effective without causing unacceptable adverse effects. Drugs with narrow therapeutic indexes have a lesser difference between doses that produce therapeutic effects and doses that cause adverse effects. In preclinical animal studies, we found the ratio between doses of RAP-219 that did not produce a toxic effect in 50 percent of the population ("TD_{50}") on the rotarod test were greater than 150 higher than those with ED_{50} for beneficial activity in the corneal kindling test. This compares favorably to that same ratio derived from preclinical animal models for other approved and widely prescribed ASMs which range from 1.3 for phenytoin to greater than 44 for levetiracetam. Thus, we believe RAP-219's potentially wider therapeutic index could translate to patients, providing sustained therapeutic benefit without intolerable side effects, improving upon the traditional ASMs.

RAP-219 Preclinical Toxicity Studies

In vivo good laboratory practice ("GLP") and non-GLP toxicology studies have also been conducted with RAP-219. In a 28-day GLP toxicology study in rats completed by Janssen, once-daily administration of RAP-219 was generally well- tolerated and no adverse effects were observed at any dose. Non-adverse effects including clinical signs were observed, and all non-adverse findings appeared to be reversible following completion of the 28-day recovery period. In a 28-day GLP toxicology study in dogs, once-daily administration of RAP-219 at doses of up to 10 mg/kg per day yielded overall exposures approximately 100-fold higher than those required to inhibit seizures in the mouse corneal kindling model. RAP-219 was generally well-tolerated and no adverse effects were observed at any dose. The non-adverse effects included CNS-related clinical signs, minor changes in a limited number of clinical pathology parameters, as well as minimal microscopic changes in the adrenal gland and thymus. All drug related RAP-219 effects observed either reversed completely or were in the process of reversing following the 28-day recovery period. Similar results were observed in 13-week toxicology studies in rats and dogs completed by us. Based on the preclinical toxicology data collected to date across these models, we believe RAP-219 has a low genotoxic potential and a favorable tolerability profile. These data supported further development through clinical investigation for once-daily oral dosing of RAP-219 up to 3 months.

Additional toxicology studies including a chronic (6-months in rats and 9-months in dogs) study as well as reproduction toxicology studies (in rats and rabbits) are ongoing to support longer-term dosing and dosing women of childbearing potential in subsequent clinical trials. In these ongoing studies, convulsion was observed in two instances. A female rabbit dosed at 40 mg/kg per day showed convulsion on the last day of the 10-day pilot tolerability or range finding study to enable GLP reproduction toxicology study. This dose level was considered not tolerated. The no observed effect level ("NOEL") dose for convulsion was 30 mg/kg per day.

A male dog in the ongoing 9-month chronic toxicology study developed convulsion following the first dose of 20 mg/kg. As demonstrated in the 28-day GLP toxicology study in dogs, the highest dose level tested in dogs and the NOEL dose for convulsion was 10 mg/kg per day. The margins for the mean maximum exposures (Cmax) from the Phase 2a proof-of-concept trial in refractory focal epilepsy dose (0.75 mg per day for 5 days followed by 1.25 mg per day) over that from the NOEL in rabbits and dogs were greater than 700-fold and 500-fold, respectively. To deal with convulsion in nonclinical studies, we plan to use one-tenth of the exposure from the no-effect dose level for convulsion as the highest exposure for clinical trials. Using this approach, we expect the margins will be greater than 70-fold and 50-fold in rabbits and dogs, respectively. Therefore, we believe the potential for convulsion risk to patients is low.

RAP-219 Phase 1 Trials in Healthy Adult Volunteers

A total of four Phase 1 trials with RAP-219 have been conducted to date to assess the safety, tolerability, pharmacodynamics and pharmacokinetics of RAP-219 in 100 healthy adult volunteers: a SAD trial; a first MAD trial; a MAD-2 trial; and a human PET trial. Final results are available for the SAD, first MAD, and MAD-2 trials and a final study report is in progress for the PET trial. In all of these trials, RAP-219 was generally well tolerated with no serious adverse events ("SAEs"). There were three treatment discontinuations (3%) that were attributed to treatment emergent adverse events ("TEAEs"), with no TEAEs greater than Grade 2. No clinically significant laboratory, electrocardiogram (ECG), or vital sign abnormalities were reported in the SAD or two MAD trials. While the final study report is in progress, TEAEs observed in the PET trial are generally consistent with other Phase 1 trials. The results of these trials indicate a safety and tolerability profile supporting continued clinical development of RAP-219.

The SAD trial had two parts. Part 1 was randomized, double-blind and placebo-controlled; and evaluated doses from 0.25 mg to 3 mg; and Part 2 was an open label single cohort evaluation of the effect of a high-fat meal on the pharmacokinetics of a 1 mg single dose of RAP-219. There were five cohorts in the Phase 1 SAD trial Part 1 and each cohort consisted of six subjects who received RAP-219 and two subjects who received placebo. The pharmacokinetics of RAP-219 in the SAD Part 1 trial were consistent with the observations from the nonclinical studies, and were characterized by low clearance and a long terminal elimination half-life of approximately 8 to 14 days. The maximum exposures (Cmax) at the 2 mg and 3 mg doses corresponded to approximately 50 percent projected receptor occupancy, based on data from preclinical studies. In Part 1 of the SAD trial, all doses were generally well tolerated with no SAEs, and all drug related TEAEs were rated as mild (grade 1) or moderate (grade 2). All moderate drug-related TEAEs observed were at the two highest doses (2 mg and 3 mg) and were generally consistent with the effects seen in nonclinical toxicology studies with RAP-219; included agitation and amnesia, each reported in two subjects, and anxiety, dizziness, visual hallucination, sinus tachycardia and hypertension, each reported in one subject. In Part 2 of the SAD trial, there were six subjects who all received 1 mg of RAP-219. A modest increase in overall exposure (25 percent increase in area under the curve) and maximum exposure (42 percent increase in Cmax) were observed when RAP-219 was dosed with a high-fat, high-calorie meal. Based on the emerging safety profile and the observed food effect, we believe RAP-219 can be dosed without regard to food.

The first MAD trial was a randomized, double-blind and placebo-controlled trial and evaluated once-daily doses ranging from 0.25 mg to 1.25 mg over two or four weeks. There were five cohorts in the first MAD trial. Each cohort for the first MAD trial consisted of six subjects receiving RAP-219 and two subjects receiving a placebo. In the first MAD trial, all doses were generally well tolerated with no SAEs, all drug related TEAEs were rated as mild (grade 1), and no dose response was observed with regards to drug-related TEAEs.

The MAD-2 trial was a randomized, double-blind, placebo-controlled trial in healthy volunteers and was designed to assess dosing regimens that may accelerate the time to reach therapeutic exposure more quickly than in our first MAD trial, and to further evaluate the safety and tolerability of RAP-219 with continued dose escalation. The MAD-2 trial evaluated once-daily doses ranging from 0.5 mg to 1.75 mg. There were three cohorts in the MAD-2 trial. Each cohort for the MAD-2 trial consisted of six subjects receiving RAP-219 and two subjects receiving a placebo. In the MAD-2 trial, all doses were generally well tolerated with no SAEs, all drug-related TEAEs were rated as mild (grade 1) or moderate (grade 2) and no dose or exposure-related response was observed with regards to the incidence of TEAEs. Data from the MAD-2 trial demonstrated that dose titration was feasible after just two days of dosing at the starting dose, and that the higher dose of 1.75 mg once daily was generally well tolerated. Target exposures (those trough concentrations associated with target projected receptor occupancy in pre-clinical models) were achieved within 5 days of dosing across various dosing regimens.

Among the 48 participants exposed to RAP-219 in the two MAD trials, the most common TEAEs were headache (n=5), sinus tachycardia (n=4), and brain fog, insomnia, bowel movement irregularity, dry mouth, and medical device site reaction (n=3 each). Among the 16 participants exposed to placebo, the most common TEAEs were abdominal pain, brain fog, constipation, cough, decreased appetite, dizziness, medical device site reaction, and second-degree atrioventricular block (n=1 each).

Figure 10 below shows the pharmacokinetic profile of RAP-219 following the two highest single doses from the SAD trial, the last dose (Day 28) of the two highest dose levels (Cohorts 4 and 5) in the first MAD trial, and following the last dose (Day 28) of the highest dose level (Cohort 3) in the MAD-2 trial, along with preliminary receptor occupancy concentrations based on data from the human PET trial. Cohort 4 of the first MAD trial was dosed at 0.75 mg per day for 28 days and exceeded the preliminary human receptor occupancy level of 70% at day 28 trough. Cohort 5 of the first MAD trial was dosed at 0.75 mg per day for 5 days followed by 1.25 mg per day for 23 days. Data from Cohort 5 showed maximum exposures (Cmax) up to 3-fold higher than those achieved following the highest single dose (3 mg) in the Phase 1 SAD trial and were approximately at the human receptor occupancy level of 85% at day 28 trough. Cohort 3 of the MAD-2 trial was dosed at 0.5 mg per day for 2 days, 1.0 mg per day for 2 days, and 1.75 mg per day for 24 days. Preliminary data from this cohort suggest an approximate 4-fold increase in Cmax compared to the highest single dose (3 mg) in the SAD trial and exceeded the preliminary human receptor occupancy level of 85% (see Figure 10 below).

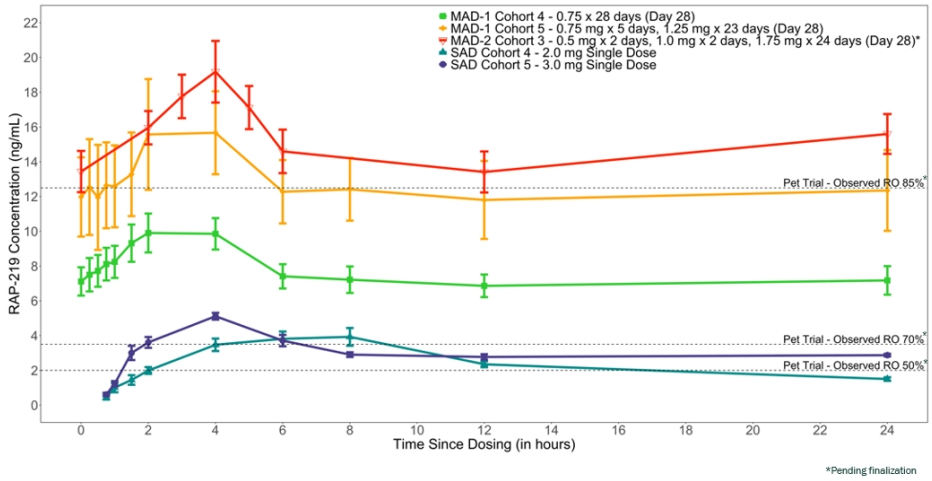


Figure 10. SAD Exposures vs. MAD Exposures.

The human PET trial was an open label trial in healthy volunteers which utilized a companion PET radiotracer to confirm brain region selectivity and brain target receptor occupancy across a range of dosing and exposure levels, and was designed to confirm neuroanatomical distribution of TARPγ8 and establish the relationship between plasma concentration and brain receptor occupancy after 14 days of dosing with RAP-219 under different dosing regimens. This trial was conducted in Belgium at a site experienced with the radiotracer. There were three cohorts in the Phase 1 PET trial: Cohort 1 was given the same dosing regimen currently being used in the Phase 2a trial in refractory focal epilepsy (0.75 mg daily for 5 days, followed by 1.25 mg daily for 9 days), and lower doses were used in the other two cohorts to better characterize the plasma concentration versus receptor occupancy relationship. Cohort 2 was given 0.25 mg daily for 14 days and Cohort 3 was given 0.25 mg daily for 7 days, followed by 0.5 mg daily for 7 days. The preliminary PET data demonstrated that Cohort 1 (the dosing regimen utilized in the ongoing Phase 2a trial in refractory focal epilepsy) exceeded the projected target receptor occupancy range associated with maximal seizure protection in preclinical models (50%-70%) within five days of dosing, while maintaining a tolerability profile generally consistent with prior Phase 1 trial findings. The trial confirmed that the expression of TARP-γ8-containing AMPA receptors is enriched in the hippocampus and cerebral cortex and is minimal in the cerebellum and brain stem.

Clinical Development Plan of RAP-219 in Refractory Focal Epilepsy

For the Phase 2a proof-of-concept, open label trial of RAP-219, we expect to enroll approximately 20 participants who have previously been implanted with an intracranial RNS system, marketed by NeuroPace, Inc. ("NeuroPace"), to monitor and manage their epilepsy. Additional key participant eligibility criteria include implantation of the RNS system at least 15 months before screening, stable device configuration, stimulation and detection settings (including the duration of "long episodes" ("LEs") recorded by the RNS system) for at least eight weeks before screening, at least an average of eight LEs per 4-week interval and at least one clinical seizure in the 8-week retrospective eligibility period, treatment with a maximum of four concomitant medications and no generalized onset seizures in the past ten years. Participants in this trial will receive a dose of 0.75 mg per day for 5 days, followed by 1.25 mg per day for the remainder of the treatment period. Our Phase 2a proof-of-concept trial design is further detailed in Figure 11 below.

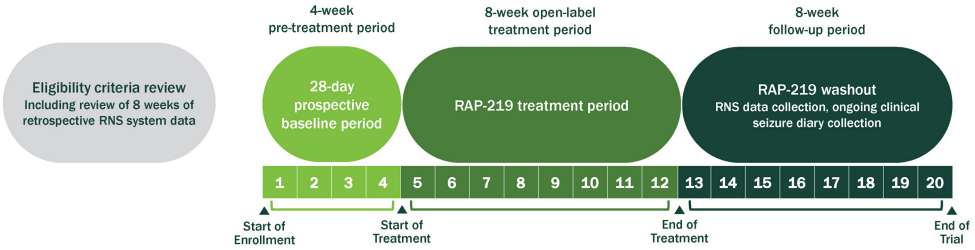


Figure 11. Phase 2a Proof-of-Concept Trial Schema.

The primary endpoint of our Phase 2a proof-of-concept trial is a reduction in frequency of LEs recorded by the RNS system, specifically the change in LE frequency during the second 4-week interval of the treatment period (weeks 5-8) compared to baseline frequency (frequency per 28 days determined across 8-week retrospective and 4-week prospective baseline intervals). One focus of this analysis will be a responder analysis to determine the proportion of participants who experience a greater than or equal to 30% decrease in long episode frequency per 28 days. The key secondary endpoints of this proof-of-concept trial include change in clinical seizure frequency (measured using patient-recorded paper diaries), change in electrographic biomarkers (including detection frequency, spike frequency, frequency of long episode with saturation, and other RNS system data outputs) and number and percent of participants who achieve any improvement as assessed by the investigator (measured by Clinical Global Impression of Change scores of minimally, much or very much improved).

In November 2023, we established a collaboration with NeuroPace to leverage the RNS system's data to track responses of patients receiving RAP-219 in our Phase 2a proof-of-concept trial. This collaboration has allowed us to more rapidly identify study sites and efficiently screen appropriate patients in the recruitment of our Phase 2a proof-of-concept trial. In addition, we believe access to NeuroPace's data collection and analysis capabilities will enable us to efficiently prepare our proof-of-concept data package.

The RNS system is FDA approved for the treatment of refractory focal epilepsy. The RNS system involves a surgeon implanting a small battery-powered device called a responsive neurostimulator in the patient's skull. The neurostimulator is connected to thin wires, or electrodes, that the surgeon places in areas of the brain where the patient's seizures originate. The device continuously records the brain's electrical activity for abnormal epileptiform patterns. Abnormal brain electrical activity detected by

the RNS system that could likely lead to a seizure is referred to as a LE. When abnormal activity is detected, the device delivers a pulse of electrical stimulation that may halt the seizure and prevent it from spreading to other brain regions. As of December 31, 2024, over 6,500 patients have been implanted with the RNS system.

Patients with the implanted RNS system typically also receive ASMs, and additional oral therapies may be prescribed to optimize treatment since many patients continue to have seizures after implantation of the device. Two retrospective studies published in peer reviewed epilepsy journals have demonstrated that when new ASMs are added to an RNS system patient's treatment regimen, LE changes detected by the RNS system within one to four weeks of new ASM treatment initiation are predictive of long-term clinical response (i.e., a clinically meaningful reduction in focal seizures) to the new ASM. In addition, other iEEG measures obtained from the RNS system have also been shown to be predictive of clinical response, such as detections or episode starts, spike frequency and spectral power, and will be used as secondary or exploratory endpoints in this trial.

Testing RAP-219 in patients with the RNS system provides the opportunity to objectively quantify changes in LE frequency as a potential biomarker of efficacy. Because LEs have been shown to provide an early and objective indicator of clinical response to an ASM, and because the population of patients with the RNS system is representative of the refractory focal epilepsy population that will be the focus of future registrational trials, quantifying LEs after the addition of RAP-219 may provide a clearer perspective on the potential of RAP-219 to provide clinical benefit in future focal epilepsy trials. We are enrolling patients who have been treated with an RNS system for at least 15 months, have stable device configuration settings, stimulation and detection settings (including LE duration) for at least eight weeks before screening and continue to have seizures while also on a stable ASM regimen. Due to an increasing number of patients in the United States implanted with an RNS system for their focal epilepsy, the support from NeuroPace in identifying patients eligible for our Phase 2a proof-of-concept trial and RAP-219's minimal drug-drug interactions observed to date, we expect to report topline results from this Phase 2a proof-of-concept trial in the third quarter of 2025 and, if the trial is positive, would provide translatable proof-of-concept for RAP-219.

The RNS proof-of-concept protocol was chosen after discussions with key opinion leaders, consultants, and clinical advisory boards, and it was determined that it provided the best chance of translatability to registrational trial outcomes in focal epilepsy. We considered other clinical models commonly used in proof-of-concept studies in epilepsy. We also considered the photosensitive epilepsy proof-of-concept model, where patients with known visually evoked epileptiform discharges are purposely provoked using a strobe light. We believe the photosensitivity model is sub-optimal because it is a single-dose study and its relevance to focal epilepsy is limited since photosensitive discharges are found in patients with generalized epilepsy. We also considered transcranial magnetic stimulation ("TMS"), where healthy volunteers are subjected to TMS and changes in TMS-evoked potentials are measured to assess cortical excitability. We believe the TMS model has limited relevance to focal epilepsy since it does not evaluate patients with epilepsy.

Assuming a successful outcome of our Phase 2a proof-of-concept clinical trial, we plan to discuss these results with the FDA and initiate registrational clinical trials to assess RAP-219 in adults with focal epilepsy. We anticipate the design of these registrational trials and patient population to be studied will be similar to those conducted for other approved therapies and, if RAP-219 is eventually approved, that RAP-219's indication will be similar to currently approved ASMs.

Opportunities to Expand the Potential for RAP-219 in Epilepsy

The ultimate goal of antiseizure therapy is complete freedom from seizures and improvement in patient quality of life. We believe that RAP-219 has the potential to significantly reduce or possibly eliminate focal epilepsy seizures while avoiding many of the common intolerable AEs associated with many approved ASMs. The differentiated target and mechanism of action of RAP-219 in combination with its neuroanatomical precision within the most common seizure onset-zones as demonstrated in preclinical models provides the opportunity for potentially superior clinical activity compared to currently approved ASMs. Certain patients who are refractory to treatment with other ASMs have been found to respond favorably to combination therapies, especially when rational polypharmacy is employed. We believe that the unique proposed mechanism of RAP-219 and its potential for reduced drug-drug interactions, if approved, would make it a drug of choice for rational polypharmacy by improving clinical benefit without changing drug levels of other ASMs.

We are also exploring the development of a long-acting injectable formulation of RAP-219 with the goal of reducing dosing frequency to once every one or two months, thereby helping to improve adherence. We envision patients would first be stabilized on an oral dose of RAP-219 and then transitioned to the long-acting injectable formulation. For many patients, nonadherence to prescribed ASMs is a major issue in optimizing benefit from pharmacotherapy. This nonadherence rate can be up to approximately 50 percent. One study found that patients who were not adherent to their ASMs had less seizure control as compared with patients who were adherent. We believe that, in addition to the potential reduced side effect profile of RAP-219, its high potency and long half-life, each observed to date in our Phase 1 studies, provide additional opportunities to improve patient adherence. In addition, we believe the potential to dose RAP-219 once per day would be preferred by patients and should improve adherence. A long-acting

formulation of RAP-219 has the potential to be the first long-acting injectable ASM. We intend to advance such a formulation into clinical development if and when we establish a tolerable and efficacious once-daily oral formulation.

Other Potential Clinical Applications for RAP-219 and TARPγ8 Modulators

Many ASMs blunt excitatory neurotransmission in the CNS and some have been shown to provide clinical benefit in other indications, including peripheral neuropathic pain and psychiatric diseases. However, the same issues that are problematic in ASMs used to treat epilepsy, such as intolerable AEs and drug-drug interactions, are also present when treating these other indications. Because monotherapy also commonly fails in the treatment of peripheral neuropathic pain and psychiatric conditions, polypharmacy is a widespread practice.

Bipolar Disorder Background and TARPγ8 as a Potential Treatment

Bipolar disorder is characterized by alternating episodes of depression and either mania (bipolar I) or hypomania (bipolar II). Bipolar Mania is characterized by discrete periods of elevated or irritable mood, increased energy, and heightened activity that represent a noticeable change from previous behavior. In bipolar I, manic symptoms are sufficient to require inpatient treatment whereas bipolar II typically involves milder hypomanic episodes that don't require inpatient treatment. Depressive symptoms in patients with bipolar depression include symptoms such as persistent sad or irritable mood, loss of interest or pleasure in nearly all activities, feelings of worthlessness or excessive guilt, diminished ability to think or concentrate, and recurrent thoughts of death or suicide. Previous manic or hypomanic symptoms in a patient with depressive symptoms defines the diagnosis of bipolar disorder; with some patients experiencing both manic and depressive symptoms in the same episode.

Bipolar disorder affects 2.8 percent of the adult population in the United States, or approximately 7.2 million adults. The global bipolar disorder market was approximately $1.4 billion in 2022, and sales are expected to grow to over $4 billion by 2028. Bipolar disorder is often treated with antipsychotic medications as a monotherapy or in combination with mood stabilizers. The side effects and safety risks associated with antipsychotic drugs in patients with bipolar disorder include dizziness, sedation, weight gain, movement disorders and agitation.

We believe that RAP-219 has the potential to provide a clinical benefit to patients with bipolar disorder for multiple reasons. First, there are several ASMs, including valproate, lamotrigine, and carbamazepine, that have shown clinical benefit in epilepsy and bipolar disorder and are FDA approved for both indications. The corneal kindling model of epilepsy is also believed by some experts to be predictive of bipolar treatments. Second, third- party functional neuro-imaging studies in patients with bipolar disorder typically show that the hippocampus, a brain region where TARPγ8 is expressed, exhibits abnormal activation and hyperactivity as well as elevated responses to emotional stimuli, attentional activities and memory tasks. Finally, a third-party genome-wide association study of 40,000 patients with bipolar disorder reported that bipolar disorder risk alleles were enriched in genes in synaptic signaling pathways and brain-expressed genes, particularly those with high specificity of expression in neurons of the prefrontal cortex and hippocampus. We believe that by selective targeting TARPγ8 and blunting abnormal hippocampal activity, RAP-219 may normalize these responses and thereby improve the symptoms of bipolar disorder.

Background of Peripheral Neuropathic Pain

Neuropathic pain is a chronic condition caused by dysfunctional or damaged nerves, classified either as peripheral or central, depending on whether the primary dysfunction or damage is in the peripheral nervous system or in the CNS. Peripheral neuropathic pain is a common condition estimated to affect up to 17 percent of the global population. Peripheral neuropathic pain is a large market, estimated at $6.6 billion globally in 2021 and forecasted to grow at over four percent annually. Peripheral neuropathic pain indications reflect large patient populations in the United States, including, for example, painful diabetic peripheral neuropathy at approximately 2.8 million, post- herpetic neuralgia at approximately 1.8 million and trigeminal neuralgia at approximately 1.0 million diagnosed patients.

It is generally accepted that peripheral neuropathic pain often begins with an injury to or dysfunction of a peripheral nerve resulting in abnormal, spontaneous activity, known as ectopic discharges, akin to epileptic activity in the brain, that results in abnormal spontaneous pain and abnormal painful and uncomfortable sensations. The ectopic discharges from peripheral nerves travel to the dorsal horn of the spinal cord and then to the brain and can cause sensitization and hyperexcitability in both the spinal cord and the brain. It is hypothesized that inflammation associated with the injury also drives chronic stimulation of neurons, leading to prolonged sensations of pain. Although peripheral neuropathic pain may start with dysfunction or damage in the peripheral nervous system, aberrant signaling into the spinal cord generally progresses with functional chronic changes to the CNS, both in the spinal cord and brain.

There is significant unmet need in the treatment of peripheral neuropathic pain, with most available treatments only having moderate efficacy and all having side effects that limit their use. First-line therapy with gabapentin or pregabalin is associated with lethargy, vertigo, cognitive issues and peripheral swelling. Opioid analgesics are typically not efficacious in peripheral neuropathic pain and are associated with nausea, lethargy, cognitive slowing and constipation. Opiates also have abuse potential that limits widespread use. Nonsteroidal anti-inflammatory drugs are often prescribed but rarely have meaningful efficacy and are associated with gastrointestinal, renal and cardiovascular AEs.

Evidence for the Importance of AMPARs and TARPγ8 in Pain

TARPγ8 is expressed in areas of the CNS associated with pain including the anterior cingulate cortex and the dorsal horn of the spinal cord. It is hypothesized that the anterior cingulate cortex registers affective aspects of pain while the dorsal horn processes nociceptive inputs from peripheral nerves. TARPγ8 inhibition has demonstrated preclinical activity in third party pain models. For instance, a TARPγ8 AMPAR selective inhibitor, LY3130481, was found by third-party researchers to suppress excitatory synaptic transmission in pain pathways and significantly reduce pain-related behaviors in mouse models of neuropathic and inflammatory pain without impairing motor function. This study also reported that the magnitude of improved pain behavioral effects were positively correlated with occupancy of TARPγ8 containing AMPARs in the CNS and were lost in TARPγ8 knock-out mice, supporting the dependence of the antinociceptive action of LY3130481 on TARPγ8.

Our preclinical studies with RTX-1738 have demonstrated pain behavior improvements in animal models of acute, inflammatory and neuropathic pain. In the rat formalin induced pain model, we observed that RTX-1738 administered 60 minutes before formalin attenuated nocifensive behavior during both phase 1 (acute pain, 0-10 minutes after formalin injection) and phase 2 (persistent pain, 20-60 minutes after formalin injection). In another study, RTX-1738 showed attenuation of tactile allodynia in the spinal nerve ligation ("SNL") rat model of neuropathic pain. In this test, RTX-1738 was administered daily 7 days after nerve ligation, and pain behavior was assessed 90 minutes post-dose. Starting at day 16 after surgery, which corresponds to day three of dosing with RTX-1738, paw withdrawal threshold was elevated, reflecting a decrease in pain behavior.

There has also been encouraging evidence from prior clinical trials of perampanel in neuropathic pain associated with diabetic neuropathy and post-herpetic neuralgia. While the randomized placebo-controlled studies failed to show a significant reduction in pain scores, subjects that tolerated perampanel reported moderate but meaningful pain relief in the subsequent open-label study. We believe that the trial's failure to show reduction in pain in the overall population was likely driven by perampanel's intolerable AEs.

Our nAChR Programs

We have a portfolio of discovery projects that leverage RAPs for nAChRs that we believe have potential for generating product candidates. Neuronal AChRs are transmembrane ligand-gated ion channels composed of five subunits of α/β subtypes. These receptors are excitatory acetylcholine gated ion channels and are expressed throughout the CNS as well as the periphery. They have critical roles in diverse aspects of neuronal signaling in the central and autonomic nervous system. We are optimizing nAChR modulators in anticipation of selecting candidates to advance into the clinic.

Our α6 nAChR Program

We are developing agonists and PAMs of the α6 nAChR in chronic pain, which may include neuropathic pain, inflammatory pain and nociceptive pain. Pan-nAChR agonists have been shown to significantly reduce pain in third-party clinical trials, but these agonists were associated with side effects that have limited their development potential. We believe that our RAP platform technology, which allows identification of agonists and PAMs that are selective for α6 nAChR, has the potential enable the discovery of molecules with clinical activity in pain and improved tolerability.

α6 nAChR as a Potential Target in Chronic Pain

Nicotine and certain nAChR agonists have analgesic properties, but their development for chronic pain has been unsuccessful. Epibatidine, a naturally occurring compound, is a pan-nAChR agonist with high affinity for α4β2 and α3β4 nAChRs, the most widely expressed subtypes in the mammalian nervous system. Epibatidine has potent analgesic properties. However, it is associated with toxic side effects that have precluded its development. ABT-594, an investigational third-party pan-nAChR agonist, demonstrated significant improvements in patients with neuropathic pain in a Phase 2 randomized placebo-controlled study, but up to 66 percent of patients withdrew from the trial due to AEs such as nausea, dizziness, vomiting, abnormal dreams and asthenia (weakness or lack of energy). Following these results, further development of ABT-594 was discontinued. There are currently no approved drugs for pain that specifically target nAChRs.

Third-party animal and human studies have implicated the α6 nAChR as a potential target for chronic pain. This nAChR subtype is enriched in sensory neurons of dorsal root ganglia ("DRG"), and α6 nAChR activity is associated with reduced pain. Mouse strains with increased levels of α6 in DRG showed reduced pain in a spared nerve injury ("SNI") model of neuropathic pain. Conversely, complete inactivation of the gene for α6 in mice blocked the analgesic effects of nicotinic compounds. In humans, genetic variants with reduced α6 nAChR activity showed increased levels of postoperative pain.

Although the potential for selective α6 agonists as a therapeutic agent for pain has been acknowledged, discovery efforts have been hampered by challenges in establishing functional assays for α6 containing nAChRs in cell lines. Recombinant α6 does not assemble into functional multi-subunit nAChRs; therefore, α6 activity could not be measured in cell lines used for drug discovery. Our Chief Scientific Officer, Dr. Bredt, and his colleagues, overcame this impediment through the identification of RAPs, which serve as chaperones and auxiliary subunits that drive the assembly of functional α6-containing nAChRs. This has enabled us to functionally express α6 nAChR and discover a series of α6 selective PAMs and agonists. We believe that these α6 selective nAChR PAMs and agonists have the potential to alleviate chronic pain while avoiding the AEs that have precluded development of earlier non-selective nAChRs agonists.

Preclinical Validation of Our Approach

We plan to advance our discovery-stage α6 nAChR program into further development. Janssen conducted high-throughput screen of cells engineered to express α6 nAChRs and identified PAMs that were selective for this nAChR subtype. These PAMs were further characterized in patch clamp assays where they were shown to be selective modulators of α6β4 compared to nAChRs that did not contain the α6 subunit, including the more ubiquitously expressed α4β2 and α3β4 nAChRs. One of these PAMs, RTX-2621, was a potentiator of α6β4 and had low activity on α4β2 and α3β4 nAChR subtypes.

We tested RTX-2621 in the rat SNI model for neuropathic pain. In this model, damage to the sciatic nerve results in hypersensitivity of the rat paw to stimuli. This is generally recognized to be a robust model of neuropathic pain, as it replicates many of the neuronal signaling changes and physiological responses observed in humans. It was observed that RTX-2621 mitigated this hypersensitivity. We believe this demonstrates the potential for α6 to be a therapeutic target in chronic pain.

Our α9α10 nAChR Program

Another program involves the α9α10 nAChR. We are developing an agonist to the α9α10 nAChR in hearing disorders, which may include age-related hearing loss, acoustic trauma and tinnitus, as well as vestibular disorders. Third-party genetic studies in mice have shown that augmenting the α9 nAChR pathway can help prevent hearing loss associated with aging, acoustic trauma and that this pathway also be relevant to vestibular disorders. Despite this genetic validation, discovery of selective α9α10 nAChR agonists has been challenging because recombinant nAChRs containing α9α10 in cell lines fail to create a functional receptor. Our ability to identify agonists that are selective for α9α10 nAChR was made possible by the application of our RAP platform technology. We are currently developing an oral therapeutic targeting the α9α10 nAChR, which we believe has a high potential target in hearing disorders. We also believe the α9α10 nAChR is a potential target in vestibular disorders, and we may develop an oral product candidate for this indication in the future.

Background to Hearing Disorders

Hearing disorders impact a large percentage of the population. For example, approximately one third of people aged 65 to 74 and nearly half aged 75 and older have age-related hearing loss. Acoustic trauma effects approximately five percent of the global population, and surveys estimate that 10 to 25 percent of adults in the United States have tinnitus. Many hearing disorder patients start their treatment by using a hearing aid, with cochlear implantation given to the most severely affected patients. Despite this high prevalence, there are few pharmacotherapeutic treatments to prevent or reverse hearing disorders.

α9α10 nAChR as a Potential Target in Hearing Disorders

In the inner ear, the cochlea converts mechanical sound vibrations into nerve signals, which are transmitted to the brain. Sound vibrations are detected by a combination of outer hair cells, which amplify sound, and inner hair cells ("IHCs"), which receive the amplified sound signals. The IHCs, in turn, translate the incoming signals into release of neurotransmitters, which traverse the synapse to stimulate neurons that send electrochemical signals to the brain. One of the key receptors in this process is the α9α10 nAChR, which is highly enriched in cochlear hair cells.

The role of the α9α10 nAChR in hearing loss has been demonstrated by third-party genetic experiments. Gain and loss of function mutations to the gene encoding α9 demonstrated its role in experimentally induced hearing loss. In these experiments, the thresholds to elicit auditory brain stem responses ("ABR") to various frequencies of sound were found to be elevated one day after auditory trauma, consistent with hearing loss. In wild-type mice, this effect of auditory trauma was temporary and after seven days, the ABR profile returned to that observed prior to the insult. In mice with a null mutation of the gene encoding α9, the ABR threshold was increased at day one, and this increase persisted at day seven, demonstrating increased vulnerability to hearing loss. By contrast, mice with a gain-of-function mutation in the gene for α9 were protected from any significant change in ABR on either day one or day seven.

We believe that a selective modulator of the α9α10 nAChR may help treat hearing disorders while avoiding many of the side effects that have limited the clinical application of other nAChR compounds.

Preclinical Validation of Our Approach

In vitro studies of α9α10 nAChR physiology have been challenging because this receptor could not be functionally expressed in recombinant cell lines in the absence of it RAPs. Through a genome-wide screen using our discovery platform, RAPs that drive the assembly of functional α9α10 nAChRs were identified by Janssen. Expression of these RAPs along with the α9 and α10 subunits enabled functional α9α10 nAChR expression in cell lines that we believe are suitable for drug discovery.

Janssen conducted a high throughput screen of cells engineered to express α9α10 nAChR and identified a number of small molecule agonists of α9α10. Through our medicinal chemistry efforts, α9α10 agonists with low nanomolar potency, inner ear penetration and high selectivity versus other nAChR family members have been identified and are being optimized. The use of these orally administered molecules in physiological hearing models may demonstrate the potential of α9α10 agonists to address hearing disorders.

Manufacturing and Supply

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 ("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 biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe our product candidates, platform, knowledge, experience and scientific personnel provide us with competitive advantages, we face potential competition from many different sources, including large and small pharmaceutical and biotechnology companies, academic institutions and governmental agencies as well as public and private research institutions. Any product candidates that we successfully develop and commercialize, including RAP-219, may compete with existing therapies and new therapies that may become available in the future.

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

The key competitive factors affecting the success of RAP-219, and any other product candidates that we develop to address focal epilepsy and other neurological and psychiatric 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.

Focal Epilepsy

In the field of focal epilepsy, we face competition from a variety of currently marketed therapies such as generic anticonvulsants, ASMs, sodium channel modulators and benzodiazepines, devices such as deep brain stimulation like the RNS system as well as brain surgeries in patients who have failed polypharmacy. RAP-219 may face competition from currently marketed therapies such as XCOPRI (cenobamate), which was developed by SK Life Science Inc. and approved by the FDA in November 2019 and FYCOMPA (perampanel), which was developed by Eisai Co. Ltd. and approved by the FDA in 2012. Our competition for RAP-219 may also include therapies in clinical development, such as XEN1101 being developed by Xenon Pharmaceuticals Inc., BHV-7000 being developed by Biohaven Ltd. ("Biohaven"), PRAX-628 being developed by Praxis Precision Medicines, Inc., darigabet being developed by Cerevel Therapeutics Holdings, Inc., ES-481 being developed by ES Therapeutics Australia Pty Ltd., SPN-817 being developed by Supernus Pharmaceuticals, Inc. and ADX71149 being developed by Addex Therapeutics Ltd. in partnership with Janssen Pharmaceuticals, Inc.

Bipolar Disorder

In the field of bipolar disorder, RAP-219 faces competition from mood stabilizers (e.g. lithium and Lamictal) and antidepressants (e.g. selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors). Our competition may also include other programs in clinical development for the treatment of disorder in bipolar disorder, such as BHV-7000 being developed by Biohaven.

Peripheral Neuropathic Pain

In the field of peripheral neuropathic pain, our principal competition is from existing therapies, which include antidepressants (e.g., duloxetine, venlafaxine, amitriptyline and other tricyclic drugs), gabapentinoids (e.g., gabapentin, pregabalin), and opioids (e.g., tapentadol hydrochloride). We are also aware that various therapies are used off-label to treat peripheral neuropathic pain. Our competition may also include other programs in clinical development in peripheral neuropathic pain, such as VX-548 being developed by Vertex, Inc., LX9211 being developed by Lexicon Pharmaceuticals, Inc. and BHV-2100 being developed by Biohaven.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We may also rely on trademarks, copyrights and trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary and intellectual property position. We additionally may rely on regulatory and other protections afforded through data exclusivity, market exclusivity and patent term extensions, where available.

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

The patent positions for biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

TARPγ8 Program

We own six patent families directed to TARPγ8 modulators. A first patent family is directed to compositions of matter of certain TARPγ8 modulators, including RAP-219, and methods of use and expires in 2036, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. patent, one European patent, validated in 40 states, over 25 patents in various other foreign jurisdictions, two U.S. pending application, and over 10 applications pending in foreign jurisdictions. A second patent family is directed to compositions of matter of certain TARPγ8 modulators and methods of use and expires in 2037, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. patent. A third patent family is directed to compositions of matter of certain TARPγ8 modulators and methods of use and expires in 2037, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. patent, one European patent, validated in eight states, over 10 patents in various other foreign jurisdictions, and one application pending in a foreign jurisdiction. A fourth patent family is directed to compositions of matter of certain TARPγ8 modulators and methods of use and expires in 2037, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. patent, one European patent, validated in six states, more than 10 patents in various other foreign jurisdictions, and three applications pending in foreign jurisdictions. A fifth patent family is directed to crystalline forms of a TARPγ8 modulator and methods of use and expires in 2045, if granted, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one pending international application filed under the Patent Cooperation Treaty. A sixth patent family is directed to methods of use and oral doses of a TARPγ8 modulator and expires in 2045, if granted, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one pending US provisional application.

nAChR Program

We own one patent family directed to nAChR modulators. This patent family is directed to compositions of matter of certain nAChR modulators and methods of use and expires in 2046, if granted, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one pending US provisional application.

We have also non-exclusively in-licensed from Janssen Pharmaceutica NV three patent families directed to recombinant cells for the expression of nAChRs. A first patent family is directed to expression systems for the α9α10 nicotinic acetylcholine receptor and methods of use and expires in 2040, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. pending application and three applications pending in foreign jurisdictions. A second patent family is directed to expression systems for the α2α5β2 nicotinic acetylcholine receptor and methods of use and expires in 2042, if granted, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. pending application and multiple applications in foreign jurisdictions. A third patent family is directed to α6β4 nicotinic acetylcholine receptor and methods of use and expires in 2042, if granted, without taking a potential patent term extension into account. As of March 1, 2025, this patent family has one U.S. pending application and multiple applications in foreign jurisdictions.

The term of individual patents depends upon 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 a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended, and a given patent may only be extended once. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. If our product candidates receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved product candidates. We also intend to seek patent term

extensions in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we also rely on know-how and trade secret protection for our proprietary information to develop and maintain our proprietary position. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors and potential collaborators, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our know-how, trade secrets, and other proprietary information.

In addition, we plan to rely on regulatory protection based on drug exclusivities, data exclusivities, and market exclusivities. See the section titled "*—Government Regulation*" for additional information.

License and collaboration agreements

Option and License Agreement with Janssen Pharmaceutical NV

In August 2022, we entered into an option and license agreement with Janssen Pharmaceutical NV, as amended on April 3, 2023, April 18, 2023, May 2, 2023, October 2, 2023, and April 9, 2024 (collectively, the "Janssen License"), under which we received an exclusive option to obtain from Janssen (a) a worldwide exclusive license for the research, development, and commercialization of transmembrane TARPγ8 AMPAR products for the diagnosis, treatment, prophylaxis or palliation of any disease or condition in humans or other animals (the "Field") and (b) an assignment of certain patents related to TARPγ8, in each case of (a)-(b), subject to certain retained rights by Janssen. Pursuant to the Janssen License, we also received a worldwide, royalty-free, non-exclusive license (exclusive under certain joint patents) for the research, development, and commercialization of certain neuronal nicotinic acetylcholine ("nACh") products in the Field.

We made a non-refundable, non-creditable upfront payment of $1.0 million to Janssen after we entered into the Janssen License. In October 2022, we exercised the option and paid a non-refundable, non-creditable option fee of $4.0 million to Janssen. If we succeed in developing and commercializing TARPγ8 products, Janssen will be eligible to receive (i) up to $76.0 million in development milestone payments and up to $40.0 million in sales milestone payments for the product containing the lead TARPγ8 development candidate, and (ii) up to $25.0 million in development milestone payments and up to $42.0 million sales milestone payments for other TARPγ8 products containing a non-lead TARPγ8 development candidate.

Janssen is also eligible to receive (a) royalties ranging from mid to high-single digit percentages on worldwide net sales of any products containing a TARPγ8 development candidate and (b) royalties ranging from low to mid-single digit percentages for other TARPγ8 products that do not contain a TARPγ8 development candidate, in each case of (a) and (b), subject to potential reductions following the expiration of valid claims and regulatory exclusivity covering such TARPγ8 products, the launch of certain generic products and the application of certain anti-stacking reductions for third party intellectual property payments, subject to a customary reduction floor. The royalties for any TARPγ8 product will expire on a country-by-country basis upon the latest to occur of (i) the expiration of all valid patent claims covering such product in such country, (ii) the expiration of all regulatory exclusivities in such country, and (iii) a specified number of years following the first commercial sale of such product in such country. The Janssen License provides us with certain other exclusive rights with respect to small molecules with activity against TARPγ8 and nACh.

We have the right to terminate the Janssen License for any or no reason upon providing prior written notice to Janssen upon ninety (90) days' prior written notice to Janssen. Either party may terminate the license agreement in its entirety for the other party's material breach if such party fails to cure the breach or upon certain insolvency events involving the other party.

NeuroPace Master Services Agreement and Statement of Work

In November 2023, we entered into a master services agreement (the "NeuroPace Agreement") with NeuroPace Inc. ("NeuroPace"), the manufacturer and distributor of the responsive neurostimulation ("RNS") system. Pursuant to the NeuroPace Agreement and in accordance with statement of work agreements entered into from time to time, NeuroPace provides us with certain services with respect to data from the RNS systems used in our clinical trials. The NeuroPace Agreement also grants us a royalty-free, worldwide, exclusive, non-transferable license to all data collected by the RNS systems in our Phase 2a clinical trial and the outcomes of algorithms that are applied to such data, as well as the ability to publish the outcomes of algorithms, subject to certain conditions. The consideration we will pay to NeuroPace for such services is set out in each statement of work agreement.

The NeuroPace Agreement contains an exclusivity provision providing that, at any time while providing services under the NeuroPace Agreement and for a period after the final clinical study report, NeuroPace may not perform any services that are the same as the services covered by the NeuroPace Agreement to any business that directly competes with us, subject to the specific

terms of the NeuroPace Agreement. The NeuroPace Agreement also contains standard representations and warranties, confidentiality and intellectual property protective provisions and indemnification terms.

The NeuroPace Agreement expires on the later of three years from the effective date or the completion of all services under all statement of work agreements entered into prior to the third anniversary of the effective date. Either party may terminate the NeuroPace Agreement or any statement of work agreement (i) without cause by giving written notice to the other party within a specified period of time, (ii) by giving written notice upon a curable material breach that is not remediated within a specified period of time, or (iii) immediately upon written notice in the event of a material breach that cannot be cured.

Concurrently with the execution of the NeuroPace Agreement, the parties also entered into an initial statement of work, as amended in March 2024 (the "NeuroPace SOW"), under the NeuroPace Agreement, pursuant to which NeuroPace agreed to provide services related to our Phase 2a clinical trial of RAP-219, including, among other things, clinical trial readiness support, identification of potential patients satisfying the enrollment criteria and RNS system data reporting and data analysis. Pursuant to the payment schedule set out in the NeuroPace SOW, we will pay NeuroPace an aggregate of up to $3.7 million over a period of approximately two years in connection with NeuroPace's provision of services and achievement of certain patient enrollment and deliverable milestones.

Government Regulation

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

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the U.S. Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the U.S. Department of Justice or other governmental entities. In addition, an applicant may need to recall a product.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

•completion of nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP regulations;

•submission to the FDA of an investigational new drug application ("IND") which must take effect before human clinical trials may begin;

•approval by an institutional review board ("IRB") representing each clinical site before each clinical trial may be initiated at that site;

•performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCPs") to establish the safety and efficacy of the proposed drug product for each indication;

•preparation and submission to the FDA of a New Drug Application ("NDA") and payment of user fees;

•review of the product by an FDA advisory committee, where appropriate or if applicable;

•satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;

•satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;

•FDA review and approval of the NDA; and

•compliance with any post-approval requirements, including risk evaluation and mitigation strategies ("REMS") and post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a compound in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient ("API") and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. Some long-term preclinical testing, such as animal tests of reproductive adverse effects and carcinogenicity, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of the investigational drug. In an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments. In addition, the results of the preclinical tests, manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. The FDA also may impose a clinical hold or partial clinical hold after commencement of a clinical trial under an IND. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation (or full investigation in the case of a partial clinical hold) may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study is conducted in accordance with GCP, including review and approval by an independent ethics committee ("IEC") and informed consent from subjects. The GCP requirements are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. FDA must also be able to validate the data from the study through an on-site inspection if necessary.

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

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health ("NIH") for public dissemination on its ClinicalTrials.gov website.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects, or their legal representative, provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

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

•*Phase 1*. The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine maximal dosage.

•*Phase 2*. The drug is administered to a limited patient population to identify possible AEs and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

•*Phase 3*. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Post-approval studies, often referred to as Phase 4 studies, may be conducted after initial regulatory approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. In addition, within 15 calendar days after the sponsor determines that the information qualifies for reporting, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a significant application user fee as well as annual prescription drug product program fees. These fees are typically increased annually. Certain exceptions and waivers are available for some of these fees.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt, before accepting the NDA for filing, to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Applications for drugs containing new molecular entities are meant to be reviewed within 10 months from the date of filing, and applications for "priority review" products containing new molecular entities are meant to be reviewed within 6 months of filing.

The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

During its review of an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA, including drug component manufacturing (such as APIs), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an NDA unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential AEs, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use ("ETASU"). ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries.

The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product.

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

Fast Track, Breakthrough Therapy, and Priority Review

The FDA has a number of programs intended to facilitate and expedite development and review of new drugs if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. Three of these programs are referred to as Fast Track Designation, Breakthrough Therapy Designation, and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track Designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate an NDA review for a priority review if it is for a product that treats a serious or life-threatening disease or condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from 10 months to 6 months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality ("IMM"), and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly.

The accelerated approval pathway is contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Sponsors are also required to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the sponsor fails to conduct such studies in a timely manner and send the necessary updates to the FDA, or if a confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for product candidates approved under accelerated regulations, which could adversely impact the timing of the commercial launch of the product.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities and select clinical trial sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If a complete response letter is issued, the applicant may resubmit the NDA to address all of the deficiencies identified in the letter, withdraw the application, or request a hearing. If the applicant resubmits the NDA, the FDA will issue an approval letter only when the deficiencies have been addressed to the FDA's satisfaction. The FDA has committed to reviewing such resubmissions in 2 or 6 months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety or effectiveness after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, reporting of adverse experiences with the product and applicable product tracking and tracing requirements. After approval, many changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are annual prescription drug product program fee requirements for certain marketed products.

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

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

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

From time to time, legislation is drafted, introduced, passed in Congress and signed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidance, and policies are often revised or reinterpreted by the agency in ways that may significantly affect the manner in which pharmaceutical products are regulated and marketed.

Hatch-Waxman Amendments

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application ("ANDA"). An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product, known as a reference listed drug ("RLD"). ANDAs are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through *in vitro*, *in vivo*, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

Non-Patent Exclusivity

Under the Hatch-Waxman Amendments, the FDA may not approve (or in some cases accept) an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity ("NCE"). For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, which states the proposed generic drug will not infringe one or more of the already approved product's listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity for non-NCE drugs if the NDA or a supplement to the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application or supplement. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication, but it generally would not protect the original, unmodified product from generic competition. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it only prevents FDA from approving such ANDAs.

A drug product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds 6 months to existing exclusivity periods for all formulations, dosage forms, and indications of the active moiety and to patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection and patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study, provided that at the time pediatric exclusivity is granted there is not less than 9 months of term remaining.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval, each of the patents listed by the NDA sponsor is published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Upon submission of an ANDA or 505(b)(2) NDA, an applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book that:

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- such patent has expired;
- the date on which such patent expires; or
- such patent is invalid, unenforceable or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted.

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired. If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification the applicant must send notice of the paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. If the drug has NCE exclusivity and the ANDA is submitted four years after approval, the 30-month stay is extended so that it expires seven and a half years after approval of the innovator drug, unless the patent expires or there is a decision in the infringement case that is favorable to the ANDA applicant before then.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch- Waxman Amendments, which permits a patent term restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date, provided the sponsor acted with diligence. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question and within 60 days of drug approval. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office ("USPTO") reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows similar lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires a submission to the relevant competent authorities of a marketing authorization application ("MAA") and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

In the EU, an applicant for authorization of a clinical trial must obtain prior approval from the national competent authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the relevant independent ethics committee has issued a favorable opinion. In April 2014, the Clinical Trials Regulation, (EU) No 536/2014 (the "Clinical Trials Regulation") was adopted in the EU. The Clinical Trials Regulation is directly applicable in all the EU Member States and repealed the Clinical Trials Directive 2001/20/EC, as of January 31, 2022.

The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, known as the "Clinical Trials Information System"; a single set of documents to be prepared and submitted for the application, as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by an elected Reference Member State, with support of the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (the "Member States Concerned").

Part II is assessed separately by each Member State Concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure continues to be governed by the national law of the concerned EU Member State, however, overall related timelines are defined by the Clinical Trials Regulation.

Marketing Authorization

To obtain a marketing authorization for a product in the EU, an applicant must submit an MAA either under a centralized procedure administered by the European Medicines Agency ("EMA") or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure or mutual recognition procedure) for obtaining a marketing authorization in multiple EU Member States. A marketing authorization may be granted only to an applicant established in the European Economic Area ("EEA") (which is comprised of the EU Member States plus Norway, Iceland and Liechtenstein).

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EEA. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue-engineered products) and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of HIV, AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the centralized procedure, the Committee for Medicinal Products for Human Use ("CHMP") established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from a public health perspective and in particular from the point of view of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, excluding clock stops, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 67 days from the date of the CHMP opinion, the European Commission will adopt its final decision on the MAA.

The decentralized marketing authorization procedure allows an applicant to apply for simultaneous authorization in more than one EU Member State of medicinal products that have not yet been authorized in any EU Member State and that do not fall within the mandatory scope of the centralized procedure.

The mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of another EU Member State. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Pediatric Development

Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan ("PIP") covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the product for which a marketing authorization is being sought. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of the protection under a supplementary protection certificate ("SPC") provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires, even where the trial results are negative. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Data and Market Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar (abbreviated) marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the EU. During an additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained a marketing authorization based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) either (i) such condition affects no more than five in ten thousand persons in the EU when the application is made, or (ii) without the benefits derived from orphan status, it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment in its development and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product would be of significant benefit to those affected by that condition.

An orphan designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized EU marketing authorization. Marketing authorization for an orphan medicinal product leads to a ten-year period of market exclusivity being granted following marketing approval of the orphan product. During this market exclusivity period, the EMA, the European Commission or the competent authorities of the EU Member States may only grant marketing authorization to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized orphan product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized orphan product consents to a second medicinal product application; or (iii) the marketing authorization holder for the authorized orphan product cannot supply enough orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation because, for example, the product is sufficiently profitable not to justify market exclusivity. Orphan designation must be requested before submitting an application for marketing approval. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Periods of Authorization and Renewals

A marketing authorization has an initial validity of five years. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State for a nationally authorized product. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least 9 months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authorities of the relevant Member States decide, on justified grounds relating to pharmacovigilance, to proceed with one further five year renewal period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for centrally-authorized products) or on the market of the authorizing EU Member State (for nationally-authorized products) within three years after authorization ceases to be valid (the so-called "sunset clause").

Regulatory Requirements after a Marketing Authorization has been Obtained

Where an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

•Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

•The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive (EU) 2017/1572, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and APIs, including the manufacture of APIs outside of the EU with the intention to import the APIs into the EU.

•The marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of products and/or the general public, are strictly regulated in the EU notably under Directive 2001/83/EC, as amended, and EU Member State laws.

All of the aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval, and, in April 2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom ("UK") ceased being a Member State of the EU on January 31, 2020. As a result of the Northern Ireland Protocol, following Brexit, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (England, Wales and Scotland). On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework." The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the EU centralized procedure. A single UK-wide marketing authorization will be granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. However, although a separate authorization is now required to market medicinal products in the UK, under an international recognition procedure which was put in place by the MHRA on January 1, 2024, the MHRA may take into account decisions on the approval of a marketing authorization from the EMA (and certain other regulators) when considering an application for a UK marketing authorization.

There is now no pre-marketing authorization orphan designation in the UK. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the UK market, i.e., the prevalence of the condition in UK (rather than the EU) must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in the UK.

Following the end of the Brexit transition period, the MHRA continues to authorize clinical trials in the UK. The UK has implemented the now-repealed Clinical Trials Directive into national law through the Medicines for Human Use (Clinical Trials) Regulations 2004. However, on December 12, 2024, the UK government introduced a legislative proposal – the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2024 – that, if implemented, will replace the current regulatory framework for clinical trials in the UK. The legislative proposal aims to provide a more flexible regime to make it easier to conduct trials in the UK and increase the transparency of clinical trials conducted in the UK. This includes a notification scheme to enable lower-risk clinical trials to be automatically approved by the MHRA, where the risk is similar to that of standard medical care (although such trials would still require ethics committee approval). Such Regulations are expected to come into force in early 2026.

Other Healthcare Laws

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws that may affect our ability to operate include, but are not limited to:

•the federal Anti-Kickback Statute, which prohibits, among other things, persons from 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 does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs;

•federal civil and criminal false claims laws, including the False Claims Act ("FCA"), which can be enforced through civil "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the 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;

•the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new 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 these statutes without actual knowledge of the statutes or specific intent to violate them in order to have committed a violation;

•HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), imposes requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

•Even when HIPAA does not apply, according to the Federal Trade Commission ("FTC"), failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, 15 U.S.C. § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards;

•the federal Physician Payments Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA") and its implementing regulations, which requires 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 the Department of Health and Human Services ("HHS") information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed healthcare professionals (i.e., physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist

assistants, certified registered nurse anesthetists, and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

•federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

•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 and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and responsible individuals may be subject to imprisonment.

Rest of the World Regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of preclinical studies, clinical trials, product licensing, manufacturing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

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

Privacy and Data Security

In the ordinary course of business, we process sensitive data Accordingly, we are, or may be become, subject to numerous privacy and data security obligations, including global, federal, state, and local laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements and other obligations related to privacy and data security.

These privacy and data security laws are evolving and may impose potentially conflicting obligations. Such obligations may include, without limitation, federal health information privacy laws, state information security and data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., the Federal Trade Commission Act). In addition, in the past few years, numerous U.S. states have passed, or are in the process of enacting comprehensive privacy laws, rules, and regulations that impose certain obligations on covered businesses, and similar laws are being considered in several other states, as well as at the federal and state levels. While these states exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and are examples of the increasingly stringent and evolving regulatory frameworks related to personal data processing, as more fully discussed in the section titled "*Risk Factors*" included elsewhere in this Annual Report.

Additionally, to the extent we collect personal data from individuals outside of the United States, through clinical trials or otherwise, we are, or may become, subject to foreign data and data security laws, such as the European Union's General Data Protection Regulation 2016/679 ("EU GDPR") and other national data protection legislation in force in relevant EEA Member States, and the EU GDPR as it forms part UK law by virtue of section 3 of the European Union (Withdrawal) Act 2018 ("UK GDPR"). Foreign privacy and data security laws impose significant and complex compliance obligations on entities that are subject to those laws, as more fully discussed in the section titled "*Risk Factors*" included elsewhere in this Annual Report.

Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. Factors payors consider in determining coverage and reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. 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 or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost- effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical products, limiting coverage and the amount of reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. 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.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price ("ASP") and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Even if we do receive a favorable coverage determination for approved products by third-party payors, coverage policies and third-party payor reimbursement rates may change at any time.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the U.S. Centers for Medicare & Medicaid Services ("CMS") may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several U.S. Congressional inquiries and proposed and enacted state and federal 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. Congress has indicated that it will continue to seek new legislative measures to control drug costs.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

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

Current and Future U.S. Healthcare Reform

In the U.S., there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. For example, in March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, 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; and
- required manufacturers to participate in a coverage gap discount program, – later replaced under the Inflation Reduction Act of 2022 by the Medicare Part D manufacturer discount program under which manufacturers must agree to offer a 50 percent point-of-sale discount off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D (later increased to 70%); among other reforms.

Since its enactment, there have been judicial, administrative, executive, and legislative challenges to certain aspects of the ACA as well as executive orders related to the ACA's implementation. The Trump Administration is also anticipated to use executive powers to address the ACA. It is unclear how other healthcare reform measures of the Trump administration or other efforts, if any, to challenge repeal or replace the ACA, will impact our business.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, in addition to the manufacturer discount program described above, the Inflation Reduction Act of 2022 ("IRA"), among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" for such drugs and biologics under the law and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or 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. These provisions take effect progressively starting in fiscal year 2023. In August 2024, HHS completed the first round of price negotiations and announced the first set of "maximum fair prices" and the list of the first ten drugs that will be subject to such price negotiations, and HHS has announced the second round of 15 drugs to be subject to the negotiation program. The Medicare drug price negotiation program is currently subject to legal challenges. It is unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry.

Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. The IRA delayed implementation of this rule to January 1, 2032.

Other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- The U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, and, due to subsequent legislative amendments to the statute, will remain in effect until 2032.
- The U.S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers.
- The American Rescue Plan Act of 2021 eliminated the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.
- Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers were further reduced starting on January 1, 2025; however, legislation has been introduced (but not passed) in the U.S. Congress that would, if enacted, reverse these payment reductions.
- The IRA also includes several other provisions that may impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, and impose new manufacturer financial liability on all drugs in Medicare Part D.

These laws and regulations 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.

Individual states have also been increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. We expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration, any of which could limit the amounts that federal and state governments will pay for healthcare products and services.

Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the incoming Trump administration may reverse or otherwise change these measures, both the incoming Trump administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

Employees and Human Capital Resources

As of December 31, 2024, we had 69 full-time employees, and approximately 19 of our employees have M.D. or Ph.D. degrees. Within our workforce, 50 employees are engaged in research and development and 19 are engaged in business development, finance, legal, and general management and administration. Our human capital resources objectives include identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available through the "Investors" portion of our website free of charge on our website, https://investors.rapportrx.com, as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission ("SEC"). Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated by reference herein or therein. In addition, these reports may be accessed through the SEC's website, www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of business conduct and ethics, corporate governance guidelines and the charters of our audit committee, compensation committee, nominating and corporate governance committee and science technology committee are available on the "Corporate Governance" page of our investor website, https://investors.rapportrx.com.

Item 1A. Risk Factors.

Our business involves significant risks. Stockholders should carefully consider the risks and uncertainties described below and the other information in this Annual Report on Form 10-K (this "Annual Report") and in the other documents that we file with the SEC. Our business, financial condition, results of operations, or prospects could be materially and adversely affected if any of these risks occur, and as a result, the market price of our common stock could decline and stockholders could lose all or part of their investment. This Annual Report also contains forward-looking statements that involve risks and uncertainties not presently known to us or that we currently deem to be immaterial. See "Special Note Regarding Forward-Looking Statements" on page 1 for more information. Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain important factors, including those set forth below.

Risks Related to Our Limited Operating History, Financial Condition and Need for Additional Capital

We are a clinical-stage biotechnology company with a limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability. We have incurred significant financial losses since our inception and anticipate that we will continue to incur significant financial losses for the foreseeable future.

We are a clinical-stage biotechnology company with a limited operating history. We were formed in February 2022 and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our receptor associated protein ("RAP") technology platform and technology, identifying potential product candidates, securing intellectual property rights, and planning and undertaking preclinical studies and clinical trials. Substantially all of our product candidates were initially developed by Janssen Pharmaceutica NV ("Janssen"), which we in-licensed pursuant to the option and license agreement with Janssen (the "Janssen License"), entered into shortly after our formation. We have not yet demonstrated an ability to generate revenues, obtain regulatory approvals, manufacture any product on a commercial scale or arrange for a third party to do so on our behalf or conduct sales and marketing activities necessary for successful product commercialization. Our limited operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biotechnology companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

The success of our business depends primarily upon our ability to identify, develop, and commercialize product candidates based on our RAP technology platform. We do not know whether we will be able to develop any product candidates that succeed through preclinical and clinical development or products of commercial value. We have no products approved for commercial sale and have not generated any revenue from product sales to date. We will continue to incur significant research and development and other expenses related to our preclinical and clinical development and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Our net losses totaled $78.3 million and $34.8 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we have not yet generated revenues and had an accumulated deficit of $123.7 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidates.

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

- advance our product candidates through clinical development, including as we advance RAP-219 into later-stage clinical trials;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- hire additional clinical, quality control, medical, scientific and other technical personnel to support the clinical development of our product candidates;
- experience an increase in headcount as we expand our research and development organization and market development and pre-commercial planning activities;
- undertake any pre-commercial or commercial activities to establish sales, marketing and distribution capabilities;
- advance our preclinical-stage product candidates into clinical development;
- seek to identify, acquire and develop additional product candidates using our RAP technology platform, including through business development efforts to invest in or in-license other technologies or product candidates;
- maintain, expand and protect our intellectual property portfolio;

•make milestone, royalty or other payments due under the Janssen License and any future in-license or collaboration agreements; and

•make milestone, royalty, interest or other payments due under any future financing or other arrangements with third parties.

Biotechnology product development 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, secure market access and reimbursement and become commercially viable, and therefore any investment in us is highly speculative. Accordingly, before making an investment in us, our prospects, factoring in the costs, uncertainties, delays and difficulties frequently encountered by companies in clinical development, especially clinical-stage biotechnology companies such as ours, should be carefully considered. Any predictions about our future success or viability may not be as accurate as they would otherwise be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives.

Additionally, our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration (the "FDA"), European Medicines Agency ("EMA"), Medicines and Healthcare products Regulatory Agency ("MHRA") or other comparable regulatory authorities to perform clinical trials in addition to those that we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of any of our product candidates.

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

Developing biotechnology products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to continue to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek regulatory and marketing approval for, our product candidates. Even if our current or future product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. To date, we have funded our operations principally through private financings and our initial public offering ("IPO") and concurrent private placement, which closed in June 2024. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical and preclinical development of our product candidates, continue to identify additional targets using our RAP technology platform, commence additional preclinical studies and clinical trials, and continue to identify and develop additional product candidates either through internal development or through acquisitions or in-licensing product candidates.

As of December 31, 2024, we had $305.3 million of cash, cash equivalents and short-term investments, excluding restricted cash. Based upon our current operating plan, we believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements through the end of 2026. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We may also raise additional financing on an opportunistic basis in the future. For example, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates. Our future capital requirements will depend on many factors, including but not limited to:

•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 precision neuroscience approach at 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;

•the effect of macroeconomic trends including inflation and rising interest rates;

•addressing any potential supply chain interruptions or delays;

•the effect of competing technological and market developments; and

•the extent to which we acquire or invest in business, products and technologies.

Because of the numerous risks and uncertainties associated with research and development of product candidates, we are unable to predict the timing or amount of our working capital requirements. In addition, if we obtain regulatory approval for our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution which make it difficult to predict when or if we will be able to achieve or maintain profitability. Furthermore, we have incurred and expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to support our continuing operations. Our ability to raise additional funds will depend on financial, economic, political and market conditions and other factors, over which we may have no or limited control. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our product development programs, future commercialization efforts or other operations.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations with our existing cash, cash equivalents and short-term investments, any future equity or debt financings and upfront and milestone and royalty payments, if any, received under any future licenses or collaborations. If we raise additional capital through the sale of equity or convertible debt securities, or issue any equity or convertible debt securities in connection with a collaboration agreement or other contractual arrangement, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. In addition, the possibility of such issuance may cause the market price of our common stock to decline. Debt financing, if available, may result in increased fixed payment obligations and involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends or acquiring, selling or licensing intellectual property rights or assets, which could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable. Any of these occurrences may have a material adverse effect on our business, operating results and prospects.

We maintain the majority of our cash and cash equivalents in accounts with major U.S. and multi-national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions and changes in financial regulations and policies can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. In addition, changes in regulations governing financial institutions are beyond our control and difficult to predict; consequently, the impact of such changes on our business and results of operations is difficult to predict and may have an adverse effect on us.

The obligations from our license agreement with Janssen 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 the Janssen License, Janssen is entitled to substantial contingent payments upon the occurrence of certain events. For example, we will be required to pay Janssen up to $76.0 million in development milestone payments and up to $40.0 million sales milestone payments for products containing RAP-219. 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 Our Business

Our business is highly dependent on the success of our product candidates, particularly RAP-219 for focal epilepsy. If we are unable to successfully complete clinical development, obtain regulatory approval for or commercialize one or more of our product candidates, or if we experience delays in doing so, our business will be materially harmed.

To date, as an organization, we have not completed the development of any product candidates and nearly all of our candidates remain in early-stage clinical or preclinical development. Our future success and ability to generate revenue from our product candidates is dependent on our ability to successfully develop, obtain regulatory approval for and commercialize one or more of our product candidates. All of our product candidates will require substantial additional investment for clinical development, regulatory review and approval in one or more jurisdictions. If any of our product candidates, particularly RAP-219, encounter safety or efficacy problems, development delays or regulatory issues or other problems, our development plans and business would be materially harmed.

We may not have the financial resources to continue development of our product candidates if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our product candidates, including:

- our inability to demonstrate to the satisfaction of the FDA, EMA, MHRA or other comparable regulatory authorities that our product candidates are safe and effective;
- insufficiency of our financial and other resources to complete the necessary clinical trials and preclinical studies;
- negative or inconclusive results from our clinical trials, preclinical studies or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional clinical trials or preclinical studies or abandon a program;
- product-related adverse events ("AEs") experienced by subjects in our clinical trials, including unexpected toxicity results, or by individuals using drugs or therapeutic biologics similar to our product candidates;
- delays in submitting an Investigational New Drug ("IND") application or other regulatory submission to the FDA, EMA, MHRA or other comparable regulatory authorities, or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial or a suspension or termination, or hold, of a clinical trial once commenced;
- conditions imposed by the FDA, EMA, MHRA or other comparable regulatory authorities regarding the scope or design of our clinical trials;
- poor effectiveness of our product candidates during clinical trials;
- better than expected performance of control arms, such as placebo groups, which could lead to negative or inconclusive results from our clinical trials;
- delays in enrolling subjects in our clinical trials;

•high drop-out rates of subjects from our clinical trials;

•inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials;

•higher than anticipated clinical trial or manufacturing costs;

•unfavorable FDA, EMA MHRA or comparable regulatory authority inspection and review of our clinical trial sites;

•failure of our third-party contractors or investigators to comply with regulatory requirements or the clinical trial protocol or otherwise meet their contractual obligations in a timely manner, or at all;

•delays and changes in regulatory requirements, policies and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our therapies in particular; or

•varying interpretations of data by the FDA, EMA, MHRA or other comparable regulatory authorities.

In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA, and there can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

The successful development of pharmaceutical products involves a lengthy and expensive process and is highly uncertain.

Successful development of pharmaceutical products involves a lengthy and expensive process, is highly uncertain, and is dependent on numerous factors, many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

•clinical trial results may show the product candidates to be less effective than expected (for example, a clinical trial could fail to meet its primary or key secondary endpoint(s)) or have an unacceptable safety or tolerability profile;

•failure to receive the necessary regulatory approvals or a delay in receiving such approvals, which, among other things, may be caused by patients who fail the trial screening process, slow enrollment in clinical trials, patients dropping out of trials, patients lost to follow-up, length of time to achieve trial endpoints, additional time requirements for data analysis or New Drug Application ("NDA") or similar foreign application preparation, discussions with the FDA, EMA, MHRA or other comparable regulatory authority an FDA, EMA, MHRA or other comparable regulatory request for additional preclinical or clinical data (such as long-term toxicology studies) or unexpected safety or manufacturing issues;

•preclinical study results may show the product candidate to be less effective than desired or to have harmful side effects;

•post-marketing approval requirements; or

•the proprietary rights of others and their competing products and technologies that may prevent our product candidates from being commercialized.

For example, in the fourth quarter of 2024, we were notified by the FDA that the IND submitted by us for the initiation of a Phase 2a proof-of-concept trial of RAP-219 in diabetic peripheral neuropathic pain ("DPNP") was placed on clinical hold. The FDA requested additional information and amendments specific to the protocol design. We are working with the FDA to provide the requested information. Should our response to the clinical hold not be satisfactory to the FDA, the clinical hold may not be lifted on a timely basis, or at all. Furthermore, in December 2023, we withdrew the development of another TARPγ8 targeted molecule (RAP-482) in-licensed from Janssen that received a full clinical hold from the FDA prior to initiation of a Phase 1 trial, in order to prioritize development of our lead product candidate, RAP-219, and our other development candidates and programs. Furthermore, the length of time necessary to complete clinical trials and submit an application for marketing approval for a final decision by a regulatory authority varies significantly from one product candidate to the next and from one country or jurisdiction to the next and may be difficult to predict.

Even if we are successful in obtaining marketing approval, commercial success of any approved products will also depend in large part on the availability of coverage and adequate reimbursement from third-party payors, including government payors such as the Medicare and Medicaid programs and managed care organizations in the United States or country-specific governmental organizations in foreign countries, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide coverage and adequate reimbursement for our products once approved, market acceptance and commercial success would be reduced. Even if we are able to obtain coverage and adequate reimbursement for our products once approved, there may be features or characteristics of our products, such as dose preparation requirements, that prevent our products from achieving market acceptance by the healthcare or patient communities.

In addition, if any of our product candidates receive marketing approval, we will be subject to significant regulatory obligations regarding the submission of safety and other post-marketing information and reports and registration, and will need to continue to comply (or ensure that our third-party providers comply) with current Good Manufacturing Practices ("cGMPs") and Good Clinical Practices ("GCPs") for any clinical trials that we conduct post-approval. In addition, there is always the risk that we, a regulatory authority or a third party might identify previously unknown problems with a product post-approval, such as AEs of unanticipated severity or frequency. Compliance with these requirements is costly, and any failure to comply or other issues with our product candidates post-approval could adversely affect our business, financial condition and results of operations.

Due to the significant resources required for the development of our pipeline, and depending on our ability to access capital, we must prioritize the development of certain product candidates over others. Moreover, we may fail to expend our limited resources on product candidates or indications that may have been more profitable or for which there is a greater likelihood of success.

We have completed phase 1 clinical development of our lead product candidate, RAP-219, in multiple indications and are currently conducting a Phase 2a trial of RAP-219 in refractory focal epilepsy. We also intend to initiate additional Phase 2a trials of RAP-219 in bipolar mania and diabetic peripheral neuropathic pain. Our other product candidates and programs are at various stages of preclinical development. We seek to rapidly advance discovery and development of transformational small molecule medicines for patients suffering from central nervous system disorders.

Due to the significant resources required for the development of our product candidates, we must decide which product candidates and indications to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates, therapeutic areas or indications may not lead to the development of viable commercial products and may divert resources away from better opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the pharmaceutical industry, in particular for disorders of the nervous system, our business, financial condition and results of operations could be materially and adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

We may seek to grow our business through acquisitions or investments in new or complementary businesses, products or technologies, through the licensing of products or technologies from third parties or other strategic alliances. The failure to manage acquisitions, investments, licenses or other strategic alliances, or the failure to integrate them with our existing business, could have a material adverse effect on our operating results, dilute our stockholders' ownership, increase our debt or cause us to incur significant expense.

Our success depends on our ability to continually enhance and broaden our product offerings in response to changing clinician and patients' needs, competitive technologies and market pressures. Accordingly, from time to time we may consider opportunities to acquire, make investments in or license other technologies, products and businesses that may enhance our capabilities, complement our existing products and technologies or expand the breadth of our markets or customer base. Potential and completed acquisitions, strategic investments, licenses and other alliances involve numerous risks, including:

•difficulty assimilating or integrating acquired or licensed technologies, products, employees or business operations;

•issues maintaining uniform standards, procedures, controls and policies;

•unanticipated costs associated with acquisitions or strategic alliances, including the assumption of unknown or contingent liabilities and the incurrence of debt or future write-offs of intangible assets or goodwill;

•diversion of management's attention from our core business and disruption of ongoing operations;

•adverse effects on existing business relationships with suppliers, sales agents, health care facilities, surgeons and other health care providers;

•risks associated with entering new markets in which we have limited or no experience;

•potential losses related to investments in other companies;

•potential loss of key employees of acquired businesses; and

•increased legal and accounting compliance costs.

We do not know if we will be able to identify acquisitions or strategic relationships we deem suitable, whether we will be able to successfully complete any such transactions on favorable terms, if at all, or whether we will be able to successfully integrate any acquired business, product or technology into our business or retain any key personnel, suppliers, sales agent, health care facilities, physicians or other health care providers. Our ability to successfully grow through strategic transactions depends upon our ability to identify, negotiate, complete and integrate suitable target businesses, technologies or products and to obtain any necessary financing. These efforts could be expensive and time-consuming and may disrupt our ongoing business and prevent management from focusing on our operations.

To finance any acquisitions, investments or strategic alliances, we may choose to issue shares of our common stock as consideration, which could dilute the ownership of our stockholders. If the price of our common stock is low or volatile, we may be unable to consummate any acquisitions, investments or strategic alliances using our common stock as consideration. Additional funds may not be available on terms that are favorable to us, or at all.

We, our collaborators and our service providers are, or may become, subject to a variety of stringent and evolving privacy and data security laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations related to privacy and data security. Any actual or perceived failure to comply with such obligations could expose us to significant fines or other penalties and otherwise harm our business and operations.

In the ordinary course of our business, we and the third parties upon which we rely (such as our third party contract research organizations ("CROs") and other contractors and consultants) collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, sensitive third-party data, business plans, transactions, financial information and data we collect about trial participants in connection with clinical trials (collectively, sensitive data). Our data processing activities subject us to numerous evolving privacy and data security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to privacy and data security.

The legislative and regulatory framework for the processing of personal data worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. In the United States, numerous federal, state and local laws and regulations, including federal health information privacy laws, state information security and data breach notification laws, federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws) govern the processing of health-related and other personal data.

At the state level, numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, many of which differ from each other in significant ways, thus complicating compliance efforts, including providing specific disclosures in privacy notices and affording individuals certain rights concerning their personal data. For example, in California, the California Consumer Protection Act, or CCPA, established a comprehensive privacy framework for covered businesses by creating an expanded definition of personal information, establishing data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. While clinical trial data and information governed by HIPAA are currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope.

Similar laws have been passed and proposed in numerous states, as well as at the federal and local levels, and we expect more states to pass similar laws in the future. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. While these states exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely.

Additionally, we may be subject to new laws governing the privacy of consumer health data. For example, Washington's My Health My Data Act, which went into effect on March 31, 2024 broadly defines consumer health data, creates a private right of action to allow individuals to sue for violations of the law, imposes stringent consent requirements and grants consumers certain rights with respect to their health data, including to request deletion of their information. Connecticut and Nevada have also passed similar laws regulating consumer health data. These various privacy and data security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain other specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically. State laws are changing rapidly and there have been a number of proposals in the U.S. Congress for a new comprehensive federal data privacy law to which we may likely become subject to, if enacted.

Regulators and legislators in the U.S. are increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, the Biden Administration's executive order Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government-Related Data by Countries of Concern as implemented by Department of Justice regulations issued in December 2024, prohibits data brokerage transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions, and may result in exclusion from participation in federal and state programs.

Outside the United States, an increasing number of laws, regulations, and industry standards may govern privacy and data security. For example, the European Union's General Data Protection Regulation ("EU GDPR") and the United Kingdom's GDPR ("UK GDPR") impose strict requirements for processing personal data.

The EU GDPR and the UK GDPR (together, "GDPR") establish stringent requirements regarding the processing of personal data, including strict requirements relating to processing sensitive data (such as health data), ensuring there is a legal basis or condition to justify the processing of personal data, where required obtaining consent from individuals, transparent disclosures about how personal data is to be used, limitations on retention of information, implementing safeguards to protect the security and confidentiality of personal data, where required providing notification of data breaches, maintaining records of processing activities and documenting data protection impact assessments where there is high risk processing and taking certain measures when engaging third-party processors.

Under GDPR, companies may face temporary or definitive bans on data processing and other corrective activities, fines of up to €20 million (£17.5 million GBP) or 4% of annual global revenues, whichever is greater, and private litigation related to processing of personal data brought by data subjects or consumer protection organizations authorized at law to represent their interests. Non-compliance could also result in a material adverse effect on our business, financial position and results of operations.

In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area ("EEA") and the UK have restricted the transfer of personal data to the United States and other countries whose privacy laws are considered to provide adequate protection. Other jurisdictions may adopt similarly stringent interpretations of their 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's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in

the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. 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 of personal data out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

Although the UK is regarded as a third country under the EU GDPR, the European Commission has issued an adequacy decision recognizing the UK as providing adequate data protection and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. Likewise, the UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. However, the UK government is planning to reform its data protection law with the Data (Use and Access) Bill, which it has introduced to Parliament on 24 October 2024. These potential future changes to UK data protection laws may alter the similarities between the UK and EEA data protection regime and threaten the UK adequacy decision from the European Commission. The potential of the EU GDPR and UK GDPR further diverging in the future creates additional regulatory challenges and uncertainties for us. The lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of European personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA.

Additionally in the EU, the NIS 2 Directive ("NIS 2") is replacing the cybersecurity legal framework under the current NIS framework in the EU, aiming to ensure a high level of cybersecurity in the region. NIS 2 brings new medium and large organizations providing services in the EU within scope of the legal framework. It extends to additional sectors and expands the list of in-scope healthcare organizations, including to certain providers engaged in research and development of medicinal products. The new regime imposes direct obligations on management in respect of an in-scope organization's compliance with NIS 2, requires covered organizations to put in place certain cyber risk management measures, strengthens incident reporting requirements and provides supervisory authorities with a greater supervision ability compliance. The majority of obligations will come into force when national legislation implementing NIS 2 becomes effective in the relevant EU Member State. EU Member States had until October 17, 2024 to transpose NIS 2 into national legislation, although many countries have still not completed the transposition. As such, the cybersecurity regulatory landscape in the EU is currently fragmented and uncertain. To the extent we are subject to NIS 2, we will require additional investment of our resources in compliance programs. Under NIS 2 companies may be subject to administrative fines of up to the higher amount of €10 million or 2% of worldwide turnover.

In addition to privacy and data security laws, we are contractually subject to industry standards adopted by industry groups and may become subject to such obligations in the future. We are also bound by other contractual obligations related to privacy and data security, and our efforts to comply with such obligations may not be successful.

We publish privacy policies, and we may publish marketing materials, and other statements, such as compliance with certain certifications or self-regulatory principles, regarding privacy and data security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to privacy and data security (and consumers' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects.

We may at times fail (or be perceived to have failed) in our efforts to comply with our privacy and data security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which

could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable privacy and data 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 on processing personal data; and orders to destroy or not use personal data. 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.

Our information technology systems and infrastructure, or those of our collaborators and service providers, or our data, may be subject to cyber-attacks, cybersecurity incidents or breaches, compromises or other interruptions, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand, material disruption of our development programs and operations, or other adverse consequences.

In the ordinary course of our business, we and the third parties upon which we rely, process sensitive data, and, as a result, we and the third parties upon which we rely face a variety of evolving threats that could cause cyber-attacks, cybersecurity incidents, breaches, compromises, or other interruptions. Although we take steps to develop and maintain systems and controls designed to protect our sensitive data, systems and infrastructure, there can be no assurance that our internal technology systems and infrastructure, or those of third parties upon which we rely, will be sufficient to protect against a cyber-attack, cybersecurity breach, compromise or other incident such as an industrial espionage attack, ransomware, or insider threat attack, which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our sensitive data. 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.

The risk of a cyber-attack, cybersecurity incident, breach, compromise, or other interruption has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Such risks come from a variety of evolving threats, including but not limited to, social-engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by artificial intelligence ("AI"), telecommunications failures, earthquakes, fires, floods, and other similar threats.

Individuals engage in and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely, may be vulnerable to a heightened risk of cyber-attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our services.

We also face increased risks of a cyber-attack, cybersecurity incident, breach, compromise, or other interruption due to our reliance on internet technology and the number of our employees who work on a hybrid basis at home, in the office, or other public spaces. This may create additional opportunities for cyber criminals to exploit vulnerabilities. Additionally, 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 that were not found during due diligence of such acquired or integrated entities.

In addition, our reliance on third-party service providers could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks. We rely on third-party service providers and technologies to operate critical business systems to process sensitive data in a variety of contexts and our ability to monitor these third parties' information security practices is limited. These third parties may not have adequate information security measures in place and if our third-party service providers experience a cyber-attack, cybersecurity incident, breach, compromise, or other interruption, 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.

We may be unable to detect vulnerabilities in our information technology systems and infrastructure on a timely basis or until after a cyber-attack, cybersecurity incident, breach, compromise, or other interruption has occurred. Further, we may experience delays in developing and deploying remedial measures designed to adequately address any such identified vulnerabilities.

We have in the past experienced threats and security incidents related to our data and systems, and we may in the future experience additional threats, compromises, breaches or incidents. If we, or a third party upon whom we rely, experience a cyber-attack, cybersecurity incident, breach, compromise, or other interruption, or are perceived to have experienced a cyber-attack, cybersecurity incident, breach, compromise, or other interruption, we may experience adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including individual and group claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other potentially significant harms. 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 privacy and data security obligations.

Further, applicable privacy and data security obligations may require us to notify relevant stakeholders of a cyber-attack, cybersecurity incident, breach, compromise, or other interruption. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. In addition, cyber-attacks, cybersecurity incidents, breaches, compromises, or other interruptions may cause stakeholders (including investors and potential customers) to stop supporting our business, deter new customers from using our products, and negatively impact our ability to grow and operate our business.

If we were to experience a material cyber-attack, cybersecurity incident, breach, compromise, or other interruption that causes interruptions in our operations, it could result in a material disruption of our product development programs.

The use of new and evolving technologies, such as AI and machine learning ("ML"), in our operations, and the operations of third parties upon which we rely, may result in spending additional resources and present new risks and challenges that can impact our business including by posing security and other risks to our sensitive data, and as a result we may be exposed to reputational harm, other adverse consequences, and liability.

The use of new and evolving technologies, such as AI/ML, in our operations, and the operations of third parties upon which we rely presents new risks and challenges that could negatively impact our business. The use of certain AI/ML technologies can give rise to intellectual property risks, including compromises to proprietary intellectual property and intellectual property infringement. Additionally, several jurisdictions around the globe, including Europe and certain U.S. states, have proposed, enacted, or are considering, laws governing the development and use of AI/ML, such as the European Union's AI Act — the world's first comprehensive AI law — which has entered into force on August 1, 2024 and most provisions of which will become effective on August 2, 2026. This legislation imposes significant obligations on providers and deployers of high risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems.

Likewise, in the U.S., several states, including Colorado and California, passed laws that will take effect in 2026, to regulate various uses of artificial intelligence, including to make consequential decisions. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The U.S. Food and Drug Administration, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use AI systems governed by these laws or regulations, we will need to meet higher standards of data quality, transparency, monitoring and human oversight, and we would need to adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements, with the potential for significant enforcement or litigation in the event of any perceived non-compliance. Additionally, certain privacy laws extend rights to consumers (such as the right to delete certain personal data) and regulate automated decision making, which may be incompatible with our use of AI/ML. These obligations may make it harder for us to conduct our business using AI/ML, lead to regulatory fines or penalties, require us to change our business practices, retrain our AI/ML, or prevent or limit our use of AI/ML. For example, the Federal Trade Commission has required other companies to turn over (or disgorge) valuable insights or trainings generated through the use of AI/ML where they allege the company has violated privacy and consumer protection laws. If we cannot use AI/ML or that use is restricted, our business may be less efficient, or we may be at a competitive disadvantage.

The rapid evolution of AI/ML will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that AI/ML is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our vendors may in turn incorporate AI/ML tools into their own offerings, and the providers of these AI/ML tools may not meet existing or rapidly

evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI/ML, to engage in illegal activities involving the theft and misuse of sensitive data. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

Risks Related to the Discovery and Development of Our Current or Future Product Candidates

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

We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining regulatory approval from the FDA. Foreign regulatory authorities, such as the EMA and MHRA, impose similar requirements. The time required to obtain approval by the FDA, EMA, MHRA or other comparable regulatory authorities is inherently unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. For instance, jurisdictions outside of the United States, such as the European Union or Japan, may have different requirements for regulatory approval, which may require us to conduct additional clinical, nonclinical or chemistry, manufacturing and control studies. Moreover, the U.S. Supreme Court's July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which FDA's regulations, policies, and decisions may become subject to increasing legal challenges, delays, and/or changes. To date, we have not submitted an NDA to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. We must complete additional preclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our initial and potential additional product candidates is susceptible to the risk of failure inherent at any stage of development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of AEs that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA, EMA, MHRA or other comparable regulatory authorities that a product candidate may not continue development or is not approvable. It is possible that even if any of our product candidates have a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of such product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of, or intolerability caused by, such product candidate, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case. Serious AEs or other AEs, as well as tolerability issues, could hinder or prevent market acceptance of the product candidate at issue.

Our current and future product candidates could fail to receive regulatory approval for many reasons, including the following:

•the FDA, EMA, MHRA or other comparable regulatory authorities may disagree as to the design or implementation of our clinical trials;

•we may be unable to demonstrate to the satisfaction of the FDA, EMA, MHRA or other comparable regulatory authorities that a product candidate is safe and effective for its proposed indication;

•the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA, MHRA or other comparable regulatory authorities for approval;

•we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

•the FDA, EMA, MHRA or other comparable regulatory authorities may disagree with our interpretation of data from clinical trials or preclinical studies;

•the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA to the FDA or other submission or to obtain regulatory approval in the United States, the European Union, the UK or elsewhere;

•the FDA, EMA, MHRA or other comparable regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

•the approval policies or regulations of the FDA, EMA, MHRA or other comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of clinical trial results may result in our failing to obtain regulatory approval to market any product candidate we develop, which would substantially harm our business, results of operations and prospects. The FDA, EMA, MHRA and other comparable regulatory authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be granted for any product candidate that we develop. Even if we believe the data collected from future clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, EMA, MHRA or other comparable regulatory authorities.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

The FDA, EMA, MHRA or comparable regulatory authorities may disagree with our regulatory plan for our product candidates.

The general approach for FDA approval of a new drug is dispositive data from two or more adequate and well-controlled clinical trials of the product candidate in the relevant patient population. Adequate and well-controlled clinical trials typically involve a large number of patients, have significant costs and take years to complete. The FDA, EMA, MHRA or other comparable regulatory authorities may disagree with us about whether a clinical trial is adequate and well-controlled or may request that we conduct additional clinical trials prior to regulatory approval. In addition, there is no assurance that the doses, endpoints and trial designs that we intend to use for our planned clinical trials, including those that we have developed based on feedback from regulatory agencies or those that have been used for the approval of similar drugs, will be acceptable for future approvals. For instance, we may seek FDA regulatory flexibility and pursue marketing approval based on data from only one adequate and well-controlled clinical investigation. However, the FDA may be unwilling to apply regulatory flexibility and our clinical trial results may not support approval of our product candidates. In addition, our product candidates could fail to receive regulatory approval, or regulatory approval could be delayed, for many reasons, including the following:

•the FDA, EMA, MHRA or comparable regulatory authorities may not file or accept our NDA or marketing application for substantive review;

•the FDA, EMA, MHRA or comparable regulatory authorities may disagree with the dosing regimen, design or implementation of our clinical trials;

•the FDA, EMA, MHRA or comparable regulatory authorities may determine there is not substantial evidence of effectiveness to support approval;

•we may be unable to demonstrate to the satisfaction of the FDA, EMA, MHRA or comparable regulatory authorities that our product candidates are safe and effective for any of their proposed indications;

•the results of our clinical trials may not meet the level of statistical significance required by the FDA, EMA, MHRA or comparable regulatory authorities for approval;

•we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;

•the FDA, EMA, MHRA or comparable 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, EMA, MHRA or comparable 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;

•the FDA, EMA, MHRA or comparable regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

•the approval policies or regulations of the FDA, EMA, MHRA or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

We are dependent on a third party having accurately generated, collected, interpreted and reported data from certain preclinical studies and clinical trials that were previously conducted for our product candidates.

Substantially all of our product candidates were initially developed by Janssen, which we in-licensed pursuant to the Janssen License shortly after our formation. We entered into this license on the basis of our interpretation of the medical and scientific meaningfulness of Janssen's initial data. Therefore, we are dependent on Janssen having designed certain preclinical studies and clinical trials; conducted its research and development in accordance with the applicable protocols, legal and regulatory requirements, and scientific standards; having accurately reported the results of all preclinical studies conducted with respect to such product candidates; and having correctly collected and interpreted the data from these studies and trials. These risks also apply to any additional product candidates that we may acquire or in-license in the future. If these activities were not compliant, accurate or correct, the clinical development, regulatory approval or commercialization of our product candidates will be adversely affected and the earlier-reported results may not support data that we generate in our own preclinical or clinical work with those product candidates.

In addition, we rely in part on preclinical data using earlier generation TARPγ8 NAMs and third-party published data with other TARPγ8 NAMs for support of RAP-219. While we believe it is an accepted scientific practice to reference preclinical data generated using other molecules of the same class, it is possible that similar studies with RAP-219 would not have generated entirely consistent results and, as such, the studies performed with other molecules of the same class may not be reflective of the therapeutic potential of RAP-219.

If our clinical trials fail to replicate positive results from earlier preclinical studies or clinical trials conducted by us or third parties, we may be unable to successfully develop, obtain regulatory approval for or commercialize our product candidates.

The results observed from preclinical studies or early-stage clinical trials of our product candidates may not necessarily be predictive of the results of later-stage clinical trials that we conduct. Similarly, positive results from such preclinical studies or early-stage clinical trials may not be replicated in our subsequent preclinical studies or clinical trials. For instance, results seen in preclinical animal models of epilepsy or pain may not translate to similar results in patients, and results from our Phase 2a proof-of-concept trial in refractory focal epilepsy may not translate to clinical seizures. Furthermore, our product candidates may not be able to demonstrate similar activity or adverse event profiles as other product candidates that we believe may have similar profiles.

In addition, in our planned future clinical trials, we may utilize clinical trial designs or dosing regimens that have not been tested in prior clinical trials. For instance, our Phase 2a proof-of-concept trial in refractory focal epilepsy utilizes a novel study design due to the biomarker-based primary endpoint, intracranial electroencephalography ("iEEG") data. Specifically, iEEG data is recorded by an implanted responsive neurostimulation ("RNS") system, which includes an electrode that monitors intracranial brain waves and detects the magnitude, duration and frequency of electrographic activity associated with clinical seizures. We are not aware of any other trials that have used iEEG data as a primary endpoint and have not engaged and do not plan to engage with the FDA on the use of this endpoint in our Phase 2a proof-of-concept trial, as this trial will not be used as a registrational trial. Accordingly, the FDA, EMA, MHRA or other comparable regulatory authorities may have questions around the interpretability of this data, and iEEG data may not be translatable to a clinical seizure endpoint in future registrational trials.

There can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for drugs proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse effects or AEs.

Additionally, we may utilize an "open-label" clinical trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Our Phase 2a proof-of-concept trial in refractory focal epilepsy is an open label study. Most open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their

symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results of a product candidate when studied in a controlled environment with a placebo or active control.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA, EMA, MHRA or comparable foreign regulatory authority approval.

We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

To obtain the requisite regulatory approvals to commercialize any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. We may experience delays in completing our clinical trials or preclinical studies and initiating or completing additional clinical trials or preclinical studies, including as a result of regulators not allowing or delay in allowing clinical trials to proceed under an IND or similar foreign authorization, or not approving or delaying approval for any clinical trial grant or similar approval we need to initiate a clinical trial. We may also experience numerous unforeseen events during our clinical trials that could delay or prevent our ability to receive marketing approval or commercialize the product candidates we develop, including:

- regulators, IRBs, ethics committees or other reviewing bodies may not authorize us or our investigators to commence a clinical trial, or to conduct or continue a clinical trial at a prospective or specific trial site;
- we may not reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- we may experience challenges or delays in recruiting principal investigators or study sites to lead our clinical trials;
- the number of subjects or patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, and the number of clinical trials being conducted at any given time may be high and result in fewer available patients for any given clinical trial, or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to amend clinical trial protocols submitted to regulatory authorities or conduct additional studies to reflect changes in regulatory requirements or guidance, which may be required to resubmit to an IRB and regulatory authorities for re-examination;
- regulators or other reviewing bodies may find deficiencies with, fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplies, or the supply or quality of any product candidate or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the potential for approval policies or regulations of the FDA, EMA, MHRA or other comparable regulatory authorities to significantly change in a manner rendering our clinical data insufficient for approval.

Regulators or IRBs of the institutions in which clinical trials are being conducted may suspend, limit or terminate a clinical trial, or data monitoring committees may recommend that we suspend or terminate a clinical trial, due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, MHRA or other comparable regulatory authorities resulting in the imposition of a clinical hold, safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Negative or inconclusive results from our clinical trials or preclinical studies could mandate repeated or additional clinical trials and, to the extent we choose to conduct clinical trials in other indications, could result in changes to or delays in clinical trials of our product candidates in such other indications. We do not know whether any clinical trials that we conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our product candidates for the indications that we are pursuing. If

later-stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for our product candidates will be adversely impacted.

Our failure to successfully initiate and complete clinical trials and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates would significantly harm our business. Our product candidate development costs will also increase if we experience delays in testing or regulatory approvals and we may be required to obtain additional funds to complete clinical trials. There can be no assurance that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure or otherwise modify our trials after they have begun. For example, in the fourth quarter of 2024, we were notified by the FDA that the IND submitted by us for the initiation of a Phase 2a proof-of-concept trial of RAP-219 in DPNP was placed on clinical hold. The FDA requested additional information and amendments specific to the protocol design. We are working with the FDA to provide the requested information. Should our response to the clinical hold not be satisfactory to the FDA, the clinical hold may not be lifted on a timely basis, 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 or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if obtained.

Undesirable side effects caused by any of our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label, the inclusion of a Risk Evaluation and Mitigation Strategy, or the delay or denial of regulatory approval by the FDA, EMA, MHRA or other comparable regulatory authorities.

We may observe safety or tolerability issues beyond those we anticipate with our product candidates in ongoing or future clinical trials. For example, while no Grade 3 or higher AEs have been observed to date, it is possible that such events may occur in our ongoing RAP-219 clinical program or in our clinical programs for other product candidates. Additionally, it is possible that human subjects with focal epilepsy, bipolar disorder and peripheral neuropathic pain may experience greater side effects in our clinical program for RAP-219 than observed in healthy volunteers. We continue to learn more about our product candidates, and unfavorable pharmacology profiles, including extended half-lives, could lead to adverse outcomes or concerns by the FDA, EMA, MHRA or other comparable regulatory authorities.

Many compounds that initially showed promise in clinical or earlier-stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound. Results of future clinical trials of our product candidates could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics, despite a favorable tolerability profile observed in earlier-stage testing. At any time, we may decide to terminate or greatly narrow the target population for a clinical development program due to unacceptable side effects or safety concerns.

If unacceptable side effects arise in the development of our product candidates, we, the FDA, EMA, MHRA or other comparable regulatory authorities, the IRBs, or independent ethics committees at the institutions in which our trials are conducted, could suspend, limit or terminate our clinical trials, or the independent safety monitoring committee could recommend that we suspend, limit or terminate our trials, or the FDA, EMA, MHRA or other comparable regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. We may be unable to overcome any such suspensions or holds that are placed on our clinical trials. Treatment-emergent side effects that are deemed to be drug-related could delay recruitment of clinical trial subjects or may cause subjects that enroll in our clinical trials to discontinue participation in our clinical trials. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We may need to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in harm to patients that are administered our product candidates. Any of these occurrences may adversely affect our business, financial condition and prospects significantly.

Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects.

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 from obtaining approvals for the commercialization of our product candidates.

Any product candidate we develop and the activities associated with its development and commercialization, including its design, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States, and by the EMA, MHRA and other comparable regulatory authorities in other countries. 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 are developing or may seek to develop in the future will ever obtain regulatory approval.

We have no experience in submitting and supporting the applications necessary to gain marketing approvals and expect to rely on third-party 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 its obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, 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. 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. The FDA, EMA, MHRA and other comparable regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval that we may ultimately obtain could be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

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 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 becomes available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, topline or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or topline results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation and business prospects.

If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the development and commercialization of our product candidates may be delayed, and our business and results of operations may be harmed.

For planning purposes, we sometimes estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, receipt of marketing approval or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions which, if not realized as expected, may cause the timing of achievement of the milestones to vary considerably from our estimates, including:

•our available capital resources or capital constraints we experience;

•the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators;

•our ability to identify and enroll patients who meet clinical trial eligibility criteria;

•our receipt of approvals by the FDA, EMA, MHRA and other comparable regulatory authorities and the timing thereof;

•other actions, decisions or rules issued by regulators;

•our ability to access sufficient, reliable and affordable supplies of materials used to manufacture our product candidates;

•the efforts of our collaborators with respect to the commercialization of our product candidates; and

•the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities.

If we fail to achieve announced milestones in the timeframes we expect, the development and commercialization of our product candidates may be delayed, and our business and results of operations may be harmed.

We have concentrated our research and development efforts on the treatment of disorders of the nervous system, a field that faces certain challenges in drug development.

We have focused our research and development efforts on addressing disorders of the brain and nervous system. Efforts by pharmaceutical companies in this field have faced certain challenges in drug development. In particular, many neurological disorders, such as focal epilepsy, bipolar disorder and peripheral neuropathic pain, rely on subjective patient-reported outcomes as key endpoints. This makes them more difficult to evaluate than indications with more objective endpoints. For example, in our Phase 2a proof-of-concept trial in refractory focal epilepsy, we are using change in clinical seizure frequency (measured by patient-recorded paper diaries) as a secondary endpoint. Furthermore, these indications are often subject to a placebo effect, which may make it more challenging to isolate the effects of our product candidates. There can be no guarantee that we will successfully overcome these challenges with RAP-219, even with the use of the RNS system from NeuroPace Inc. ("NeuroPace") for primary and secondary endpoints in our Phase 2a proof-of-concept trial in refractory focal epilepsy, or our bipolar mania and diabetic peripheral neuropathic pain candidates or that we will not encounter other challenges in the development of our product candidates. Moreover, given the history of clinical failures in this field, future clinical or regulatory failures by us or others may have 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.

We may be subject to additional risks because we intend to evaluate our product candidates in combination with the standard of care for the indications that we are pursuing.

We intend to evaluate our product candidates in combination with other compounds, specifically the standard of care for the indications that we are pursuing. The use of our product candidates in combination with such other compounds may subject us to risks that we would not face if our product candidates were being administered as a monotherapy. The outcome and cost of developing a product candidate to be used with other compounds is difficult to predict and dependent on a number of factors that are outside our control. If we experience efficacy or safety issues in our clinical trials in which our product candidates are being administered with other compounds, we may not receive regulatory approval for our product candidates, which could prevent us from ever generating revenue or achieving profitability.

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

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

Patient enrollment is affected by many factors, including:

•the patient eligibility criteria defined in the protocol;

•the size of the patient population required for analysis of the trial's primary endpoints;

•the severity of the disease under investigation;

•the proximity of patients to study sites;

•the design of the trial;

•our ability to recruit clinical trial investigators with the appropriate competencies and experience;

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

•approval of new indications for existing therapies or approval of new therapies in general;

•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 drugs that may be approved for the indications that we are investigating;

•our ability to obtain and maintain patient consents; and

•the risk that patients enrolled in our clinical trials will drop out of the trials before completion.

We may experience challenges in recruiting principal investigators and patients to participate in ongoing and future clinical trials for such product candidates if we are unable to sufficiently demonstrate the potential of such product candidates to them. In addition, our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we may conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Furthermore, if significant AEs or other side effects are observed in any of our clinical trials, we may have difficulty recruiting patients to our trials and patients may drop out of our trials. Additionally, patients, including patients in any control groups, may withdraw from the clinical trial for various reasons, including but not limited to 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. Participants with CNS disorders such as bipolar disorder 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, which may or may not be related to our product candidate in clinical trial. Withdrawal of patients from our clinical trials may compromise the quality of our data.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials or our development efforts altogether. Delays in patient enrollment may result in increased costs, affect the timing or outcome of the planned clinical trials, product candidate development and approval process and jeopardize our ability to seek and obtain the regulatory approval required to commence product sales and generate revenue, which could prevent completion of these trials, adversely affect our ability to advance the development of our product candidates, cause our value to decline and limit our ability to obtain additional financing if needed.

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

We have never commercialized a product, and even if any of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to achieve sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Many of the indications for our product candidates have well-established standards of care that physicians, patients and payors are familiar with and, in some cases, are available generically. Even if our product candidates are successful in registrational clinical trials, they may not be successful in displacing these current standards of care if we are unable to demonstrate superior efficacy, safety, ease of administration and/or cost-effectiveness. For example, physicians may be reluctant to take their patients off their current medications and switch their treatment regimen to our product candidates. Further, patients often acclimate to the treatment regimen that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch due to lack of coverage and adequate reimbursement. Even if we are able to demonstrate our product candidates' safety and efficacy to the FDA and other regulators, safety or efficacy concerns in the medical community may hinder market acceptance.

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

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the product's acceptance into standard of care treatment algorithms by medical societies that could limit payor and physician uptake;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the product; and
- availability and adequacy of coverage and reimbursement from government payors, managed care plans and other third-party payors.

Any failure by one or more of our product candidates that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

If we 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 are our initial focus, as part of our longer-term growth strategy, we plan to develop other product candidates. In addition to the product candidates in our clinical-stage pipeline, we have in-licensed additional assets that are in earlier stages of development. We intend to evaluate internal opportunities from our existing product candidates or other potential product candidates, and also may choose to in-license or acquire other product candidates 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, EMA, MHRA or other comparable 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 be certain that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

In addition, we intend to devote substantial capital and resources for basic research to discover and identify additional product candidates. These research programs 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.

In the future, we may also seek to in-license or acquire product candidates or the underlying technology. The process of proposing, negotiating and implementing a license or acquisition is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

•exposure to unknown liabilities;

•disruption of our business and diversion of management's time and attention to develop acquired products or technologies;

•incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;

•higher than expected acquisition and integration costs;

•difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;

•increased amortization expenses;

•impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and

•inability to motivate key employees of any acquired businesses.

If we are unsuccessful in identifying and developing additional product candidates, either through internal development or licensing or acquisition from third parties, our potential for growth and achieving our strategic objectives may be impaired.

The number of patients with the diseases and disorders for which we are developing our product candidates has not been established with precision. If the actual number of patients with the diseases or disorders we elect to pursue with our product candidates is smaller than we anticipate, we may have difficulties in enrolling patients in our clinical trials, which may delay or prevent development of our product candidates. Even if such product candidates are successfully developed and approved, the markets for our product candidates may be smaller than we expect and our revenue potential and ability to achieve profitability may be materially adversely affected.

Our pipeline includes product candidates for a variety of neuroscience diseases. There is no precise method of establishing the actual number of patients with any of these disorders in any geography over any time period. With respect to many of the indications in which we have developed, are developing, or plan to develop our product candidates, we have estimates of the prevalence of the disease or disorder. Our estimates as to prevalence may not be accurate, and the actual prevalence or addressable patient population for some or all of those indications, or any other indication that we elect to pursue, may be significantly smaller than our estimates. In estimating the potential prevalence of indications we are pursuing, or may in the future pursue, including our estimates as to the prevalence of focal epilepsy, bipolar disorder and peripheral neuropathic pain, we apply assumptions to available information that may not prove to be accurate. In each case, there is a range of estimates in the published literature and in marketing studies, which include estimates within the range that are lower than our estimates. The actual number of patients with these disease indications may, however, be significantly lower than we believe. Even if our prevalence estimates are correct, our product candidates may be developed for only a subset of patients with the relevant disease or disorder or our product candidates, if approved, may be indicated for or used by only a subset. In the event the number of patients with the diseases and disorders we are studying is significantly lower than we expect, we may have difficulties in enrolling patients in our clinical trials, which may delay or prevent development of our product candidates. If any of our product candidates are approved and our prevalence estimates with respect to any indication or our other market assumptions are not accurate, the markets for our product candidates for these indications may be smaller than we anticipate, which could limit our revenues and our ability to achieve profitability or to meet our expectations with respect to revenues or profits.

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

The clinical and commercial landscapes for the treatment of neuroscience diseases are highly competitive and subject to rapid and significant technological change. We face competition with respect to our indications for our product candidates and will face competition with respect to any other drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drug candidates for the treatment of the indications that we are pursuing. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We believe that a significant number of product candidates are currently under development for the same indications we are currently pursuing, and some or all may become commercially available in the future for the treatment of conditions for which we are trying or may try to develop product candidates. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. See the section titled "*Business—Competition"* for examples of the competition that our product candidates face.

In most cases, we do not currently plan to run head-to-head clinical trials evaluating our product candidates against the current standards of care, which may make it more challenging for our product candidates to compete against the current standards of care due to the lack of head-to-head clinical trial data.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Accordingly, our competitors may be more successful than we may be in obtaining regulatory approval for therapies and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our therapies obsolete or non-competitive before we can recover development and commercialization expenses. If any of our product candidates are approved, it could compete with a range of therapeutic treatments that are in development. In addition, our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than our product candidates, which could render our product candidates obsolete and noncompetitive.

If we obtain approval for any of our product candidates, we may face competition based on many different factors, including the efficacy, safety and tolerability of our products, the ease with which our products can be administered, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Existing and future competing products could present superior treatment alternatives, including being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

In addition, our competitors may obtain patent protection, regulatory exclusivities or FDA approval and commercialize products more rapidly than we do, which may impact future approvals or sales of any of our product candidates that receive regulatory approval. If the FDA approves the commercial sale of any product candidate, we will also be competing with respect to marketing capabilities and manufacturing efficiency. We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, product price, reimbursement coverage by government and private third-party payors, regulatory exclusivities and patent position. Our profitability and financial position will suffer if our product candidates receive regulatory approval but cannot compete effectively in the marketplace.

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

If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates.

We currently have no marketing, sales or distribution capabilities. We intend to establish a sales and marketing organization, either on our own or in collaboration with third parties, with technical expertise and supporting distribution capabilities to commercialize one or more of our product candidates that may receive regulatory approval in key territories. These efforts will require substantial additional resources, some or all of which may be incurred in advance of any approval of the product candidate. Any failure or delay in the development of our or third parties' internal sales, marketing and distribution capabilities would adversely impact the commercialization of our product candidates.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

•our inability to recruit and retain adequate numbers of effective sales and marketing personnel;

•the inability of sales personnel to obtain access to or our failure to educate an adequate number of physicians on the benefits of any future products;

•the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

•unforeseen costs and expenses associated with creating an independent sales and marketing organization.

With respect to our existing and future product candidates, we may choose to collaborate with third parties that have direct sales forces and established distribution systems to serve as an alternative to our own sales force and distribution systems. Our future product revenue may be lower than if we directly marketed or sold our product candidates, if approved. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third parties, which may not be successful and are generally not within our control. If we are not successful in commercializing any approved products, our future product revenue will suffer and we may incur significant additional losses.

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

Risks Related to Employee Matters and Managing Growth

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of regulatory affairs and sales, marketing and distribution, as well as to continue to support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational, quality and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Our ability to develop product candidates, leverage our RAP technology platform and our future growth depends on attracting, hiring and retaining our key personnel and recruiting additional qualified personnel.

Our success depends upon the continued contributions of our key management and scientific personnel, many of whom have been instrumental for us and have substantial experience with developing therapies, identifying potential product candidates and building the technologies related to the clinical development of our product candidates. Given the specialized nature of brain diseases and our approach, there is an inherent scarcity of experienced personnel in these fields. As we continue developing our product candidates in our pipeline, we will require personnel with medical, scientific, or technical qualifications specific to each program. The loss of key personnel, in particular our Chief Scientific Officer, neuropharmacologists and neuroscientists, would delay our research and development activities. We currently do not have "key person" insurance on any of our employees. Despite our efforts to retain valuable employees, members of our team may terminate their employment with us on short notice. The competition for qualified personnel in the biotechnology and biopharmaceutical industries is intense, and our future success depends upon our ability to attract, retain, and motivate highly skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions, and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to implement our business strategy, which would have a material adverse effect on our business.

In addition, our clinical operations and research and development programs depend on our ability to attract and retain highly skilled scientists, data scientists, and engineers, particularly in Massachusetts and California. There is powerful competition for skilled personnel in these geographical markets, and we have from time to time experienced, and we expect to continue to experience, difficulty in hiring and retaining employees with appropriate qualifications on acceptable terms, or at all. Many of the companies with which we compete for experienced personnel have greater resources than we do, and any of our employees may terminate their employment with us at any time. If we hire employees from competitors or other companies, their former employers may attempt to assert that these employees or we have breached legal obligations, resulting in a diversion of our time and resources and, potentially, damages. In addition, job candidates and existing employees often consider the value of the stock awards they receive in connection with their employment. If the perceived benefits of our stock awards decline, it may harm our ability to recruit and retain highly skilled employees. If we fail to attract new personnel or fail to retain and motivate our current personnel, our business and future growth prospects would be harmed.

Risks Related to Our Dependence on Third Parties

We rely on third parties to assist in conducting our clinical trials. If they do not perform satisfactorily, we may not be able to obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon and plan to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. Our ability to complete clinical trials in a timely fashion depends on a number of key factors. These factors include protocol design, regulatory and IRB approval, patient enrollment rates and compliance with GCPs. We have opened clinical trial sites and are enrolling patients in a number of countries where our experience is limited. In most cases, we use the services of third parties, including CROs, to carry out our clinical trial-related activities and rely on such parties to accurately report their results. Our reliance on third parties for clinical development activities may impact or limit our control over the timing, conduct, expense and quality of our clinical trials. Moreover, the FDA requires us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these GCPs through periodic inspections of clinical trial sponsors, principal investigators, clinical trial sites and IRBs. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States.

We remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. Our failure or the failure of third parties to comply with the applicable protocol, legal and regulatory requirements and scientific standards can result in rejection of our clinical trial data or other sanctions. If we or our third-party clinical trial providers or third-party CROs do not successfully carry out these clinical activities, our clinical trials or the potential regulatory approval of a product candidate may be delayed or be unsuccessful. Additionally, if we or our third-party contractors fail to comply with applicable GCPs for any reason, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register certain clinical trials and post the

results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. Moreover, many CROs, including some of those that we have engaged to conduct our clinical trials, are experiencing enrollment challenges as a result of, among other things, high employee turnover driven by the post-COVID macroeconomic environment and the inexperience of new employees. Furthermore, at clinical trial sites, the availability of staff and trial participants has been limited due to a decrease in the number of clinical investigative sites across the globe. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, 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, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

In addition, we may rely on other third parties to collect, report and analyze data for our clinical trials. For example, our Phase 2a proof-of-concept clinical trial for RAP-219 in adult patients with refractory focal epilepsy relies on implantation of the RNS system from NeuroPace. NeuroPace is assisting us with clinical trial readiness, including identifying patients for enrollment in our trial, as well as services for the collection, reporting and analysis of patient data collected from the implanted RNS systems throughout the Phase 2a clinical trial. If NeuroPace does not successfully carry out its contractual obligations for any reason, meet expected deadlines, conduct our Phase 2a clinical trial in accordance with applicable law, including regulatory and data privacy requirements, or encounters issues with its RNS system, including issues that raise questions of safety, effectiveness or data integrity, or we are otherwise unable to maintain our relationship with NeuroPace, we would have to redesign and conduct a new clinical trial to evaluate RAP-219 in patients with refractory focal epilepsy and our business, financial condition and prospects would be harmed.

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 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.

Any of the third-party organizations we utilize may terminate their engagements with us under certain circumstances. The replacement of an existing CRO or other third party may result in the delay of the affected trials or otherwise adversely affect our efforts to obtain regulatory approvals and commercialize our product candidates. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, even if there are suitable replacements for one or more of these service providers, there is a natural transition period when a new service provider begins work. 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.

Our use of third parties to manufacture our product candidates, including those located outside of the United States in jurisdictions such as China, may increase the risk that we will not have sufficient quantities of our product candidates, raw materials, active pharmaceutical ingredients ("APIs") or drug products when needed or at an acceptable cost.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. Our current strategy is to outsource all manufacturing of our product candidates to third parties, including in jurisdictions outside of the United States such as China.

We currently rely on and engage third-party manufacturers to provide all of the API and the final drug product formulation of all of our product candidates that are being used in our clinical trials and preclinical studies. If we were to need an alternate manufacturer, we would incur added costs and delays in identifying and qualifying any such replacement. In addition, we typically order raw materials, API and drug product and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements with any commercial manufacturer. We may not be able to timely secure needed supply arrangements on satisfactory terms, or at all. Our failure to secure these arrangements as needed could have a material adverse effect on our ability to complete the development of our product candidates or, to commercialize them, if approved. We may be unable to conclude agreements for commercial supply with third-party manufacturers or may be unable to do so on acceptable terms. There may be difficulties in scaling up to commercial quantities and formulation of our product candidates, and the costs of manufacturing could be prohibitive.

Many of the third-party manufacturers we rely on have only recently begun working with us and have limited or no experience manufacturing our API and final drug products. If our manufacturers have difficulty or suffer delays in successfully manufacturing material that meets our specifications, it may limit supply of our product candidates and could delay our clinical trials.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third-party manufacturer to comply with applicable regulatory requirements and reliance on third parties for manufacturing process development, regulatory compliance and quality assurance;
- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- limitations on supply availability resulting from capacity and scheduling constraints of third parties;
- the failure of the third-party manufacturer to produce materials with acceptable quality on a larger scale;
- 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; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

If we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability to obtain regulatory approval for our product candidates. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA, EMA, and other comparable regulatory authorities.

Additionally, if any third-party manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or to enter into an agreement with a different manufacturer. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change third-party manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA, EMA, or other comparable regulatory authorities. We may be unsuccessful in demonstrating the comparability of clinical supplies, which could require the conduct of additional clinical trials. The delays associated with the verification of a new third-party manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third-party manufacturer may possess technology related to the manufacture of our product candidate that such third party owns independently. This would increase our reliance on such third-party manufacturer or require us to obtain a license from such third-party manufacturer in order to have another third party manufacture our product candidates.

If any of our product candidates is approved by any regulatory agency, we intend to utilize arrangements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Some of our manufacturers are located outside of the United States, including in China. There is currently significant uncertainty about the future relationship between the United States and various other countries, including China, with respect to trade policies, treaties, government regulations and tariffs. Increased tariffs or pending legislation that would impose federal contracting or federal funding limitations on parties directly using or connected to those using the services or equipment of certain foreign entities with known or alleged associations with foreign adversaries could potentially disrupt our existing supply chains and impose additional costs on our business. In particular, 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 our supplies and manufacturing. Additionally, it is

possible further tariffs may be imposed that could affect imports of any APIs used in our product candidates in the future, or our business may be adversely impacted by retaliatory trade measures taken by China or other countries, including restricted access to such raw materials used in our product candidates. Given the unpredictable regulatory environment in China and the United States and uncertainty regarding how the U.S. or foreign governments will act with respect to tariffs, international trade agreements and policies, further governmental action related to tariffs, additional taxes, contracting matters, regulatory changes or other retaliatory trade measures in the future could occur with a corresponding detrimental impact on our business and financial condition.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or voluntary recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. The facilities used by our contract manufacturers to manufacture our product candidates must be evaluated by the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA, MHRA or other comparable regulatory authorities, we may not be able to secure and/or maintain regulatory approval for our product candidates manufactured at these facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA finds deficiencies or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, EMA, MHRA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products, if approved.

The FDA, EMA, MHRA or other comparable regulatory authorities require manufacturers to register manufacturing facilities, and also inspect these facilities to confirm compliance with cGMPs.

Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, EMA, MHRA and other comparable regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval, if obtained.

Furthermore, should we decide to use any APIs in any of our product candidates that are proprietary to one or more third parties, we would need to maintain licenses to those APIs from those third parties. If we are unable to gain or continue to access rights to such APIs prior to conducting preclinical toxicology studies intended to support clinical trials, we may need to develop alternate product candidates from these programs by either accessing or developing alternate APIs, resulting in increased development costs and delays in commercialization of these product candidates. If we are unable to gain or maintain continued access rights to the desired APIs on commercially reasonable terms or develop suitable alternate APIs, we may not be able to commercialize product candidates from these programs.

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

We plan to opportunistically pursue strategic partnerships, as the advancement of our product candidates and development programs and the potential commercialization of our current and future product candidates will require substantial additional cash to fund expenses. If we believe that partnerships can accelerate the development or maximize the market potential of our product candidates, we will consider entering into product, target and/or geographic specific strategic partnerships on an opportunistic basis. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if we are able to obtain regulatory approval for product candidates from foreign regulatory authorities, we may enter into partnerships or collaborations with international biotechnology or pharmaceutical companies for the commercialization of such product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a partnership or collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed partnerships or collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the potential differentiation of our product candidate from competing product candidates,

design or results of clinical trials, the likelihood of approval by the FDA, EMA, or other comparable regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for partnership or collaboration and whether such a partnership or collaboration could be more attractive than the one with us for our product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Partnerships and collaborations are each complex and time-consuming to negotiate and document. Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Any partnership or collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential partnerships or collaborations or to otherwise develop specified product candidates. We may not be able to negotiate partnerships or collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

Furthermore, if conflicts arise between our collaborators and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Our collaborators could conduct multiple product development efforts and could develop, either alone or with others, products in related fields that are competitive with the product candidates we may develop that are the subject of these partnerships or collaborations with us.

Competing products may preclude us from entering into partnerships or collaborations with their competitors, fail to obtain timely regulatory approvals, prevent us from obtaining timely regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the partnership or collaboration efforts, including development, delivery, manufacturing and commercialization of products. Any of these developments could harm our company and product development efforts.

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

We may enter into collaborations for the development and commercialization of certain of our product candidates. If we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving our product candidates pose a number of risks, including the following:

•collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

•collaborators may not perform their obligations as expected;

•collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, which divert resources or create competing priorities;

•collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

•collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;

•a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

•disagreements with collaborators, including disagreements over proprietary rights, including trade secrets and intellectual property rights, contract interpretation, or the preferred course of development might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

•collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

•collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

•collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates or increase the product yield of its manufacturing, then our manufacturing costs 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 product candidates, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of our product candidates. 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 same quality 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 operations.

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

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as the vendors used to manufacture drug product or manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay or prevent completion of clinical trials, require conducting bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay or prevent approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

Risks Related to Government Regulation

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.

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

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

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 are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

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

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. Certain endpoint data we hope to include in any approved product labeling also may not make it into such labeling, including exploratory or secondary endpoint data such as patient-reported outcome measures. The FDA may also require a risk evaluation and mitigation strategies ("REMS") program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, EMA or other comparable regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA 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, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution 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 product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

Additionally, under the Food and Drug Omnibus Reform Act ("FDORA") sponsors of approved drugs and biologics must provide 6 months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed. The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The policies of the FDA, EMA and other comparable regulatory authorities may change and additional government regulations may

be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. In addition, the U.S. Supreme Court's July 2024 decision to overturn established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

While we may in the future seek designations for our product candidates with the FDA, EMA and other comparable regulatory authorities that are intended to confer benefits such as a faster development process, an accelerated regulatory pathway or regulatory exclusivity, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA, EMA, and other comparable regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. However, there can be no assurance that we will successfully obtain such designations for our product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Fast Track Designation for future product candidates we develop. If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track Designation. 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 be certain that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may rescind the Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development activities.

We may seek Breakthrough Therapy Designation for any product candidate that we develop. A breakthrough therapy is defined as a drug 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 currently approved 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, 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 are also eligible for accelerated approval and priority review.

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 any product candidate we develop qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation.

Even in the absence of obtaining Fast Track and/or Breakthrough Therapy Designations, a sponsor can seek priority review at the time of submitting a marketing application. The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from 10 months to 6 months. Priority review designation may be rescinded if a product no longer meets the qualifying criteria.

Where appropriate, we may secure approval from the FDA, EMA or other comparable regulatory authorities through the use of expedited approval pathways, such as accelerated approval. If we are unable to obtain such approvals, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, EMA, or other comparable regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA, or such other regulatory authorities may seek to withdraw the accelerated approval.

Where possible, we plan to pursue accelerated development strategies in areas of high unmet need. We may seek an accelerated approval pathway for our one or more of our therapeutic candidates from the FDA, EMA, or other comparable regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a therapeutic candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the therapeutic candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send status updates on such studies to the FDA every 180 days to be publicly posted by the agency, or if such post-approval studies fail to verify the drug's predicted clinical benefit. The FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress.

Prior to seeking accelerated approval, we would seek feedback from the FDA, EMA, or other comparable regulatory authorities and would otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA or BLA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent feedback from the FDA, EMA, or other comparable regulatory authorities, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval, there can be no assurance that such application will be accepted or that any approval will be granted on a timely basis, or at all. The FDA, EMA or other comparable regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type, including, for example, if other products are approved via the accelerated pathway and subsequently converted by FDA to full approval. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our therapeutic candidate would result in a longer time period to commercialization of such therapeutic candidate, could increase the cost of development of such therapeutic candidate and could harm our competitive position in the marketplace.

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

The ability of the FDA or comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies or comparable foreign regulatory authorities on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA, other government agencies or comparable foreign regulatory authorities may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. 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 employees and stop critical activities. If a prolonged government shutdown occurs, including as a result of reaching the debt ceiling, it could significantly impact the ability of the FDA to timely

review and process our regulatory submissions, which could have a material adverse effect on our business. Further, government shutdowns could impact our ability to access the public markets and obtain additional capital in the future.

Our relationships with healthcare providers and physicians and third-party payors will 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.

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. These laws include anti-kickback statutes, false claims statutes, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers. 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. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we conduct research and would sell, market and distribute our products. As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations that may affect our ability to operate may apply. For more information on healthcare laws and regulations that may impact our company, see the section titled "*Business—Government Regulation—Other Healthcare Laws".*

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state 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 and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare and privacy laws, as well as responding to possible investigations by government authorities, can be time and resource-consuming and can divert a company's attention from the business.

It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment, reputational harm and the curtailment or restructuring 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. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

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

The success of our product candidates, if approved, depends on the availability of coverage and adequate reimbursement from third-party payors. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. For more information on the laws and regulations that may impact coverage and reimbursement of our product candidates, see the section titled "*Business—Government Regulation—Coverage and Reimbursement*".

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

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

•a covered benefit under its health plan;

•safe, effective and medically necessary;

•appropriate for the specific patient;

•cost-effective; and

•neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. In the United States, the principal decisions about reimbursement for new medicines are typically made by U.S. Centers for Medicare & Medicaid Services ("CMS"). CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates, once approved. Patients are unlikely to use our product candidates, once approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of their cost. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates. 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.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. The FDA implemented regulations providing guidance for states to build and submit importation plans for drugs from Canada. On January 5, 2024, the FDA issued to Florida the first approval for a state importation plan. Several states now have pending applications with the FDA, including Colorado, Maine, New Hampshire, and New Mexico. If successfully implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives.

Moreover, increasing efforts by governmental and other third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. 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.

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

We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes

will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals or clearances of our product candidates, if any, may be.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example, (1) changes to our manufacturing arrangements, (2) additions or modifications to product labeling, (3) the recall or discontinuation of our products or (4) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. See the section titled "*Business—Current and Future U.S. Healthcare Reform*".

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical products, limiting coverage and the amount of reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. For instance, the Inflation Reduction Act of 2022 (the "IRA") includes several provisions that will impact our business to varying degrees, including provisions that allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, among others. All of our disclosed product candidates are small molecule drugs and certain of them are being developed in indications that may rely heavily on Medicare reimbursement, such as peripheral neuropathic pain. Accordingly, these new price-negotiation provisions may have a negative impact on our future revenue and profits. Further, the IRA imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our revenue generated from the sale of any approved products.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal 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. Congress has indicated that it will continue to seek new legislative measures to control drug costs.

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.

Our employees, independent contractors, consultants, 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, 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, EMA, and other comparable 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. 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.

Off-label use or misuse of our product candidates may harm our reputation in the marketplace or result in injuries that lead to costly product liability suits.

If our product candidates are approved by the FDA, we may only promote or market our product candidates in a manner consistent with their FDA-approved labeling. We will train our marketing and sales force against promoting our product candidates for uses outside of the approved indications for use, known as "off-label uses." We cannot, however, prevent a physician from using our product candidates off-label, when in the physician's independent professional medical judgment he or she deems it appropriate. Furthermore, the use of our product candidates for indications other than those approved by the FDA may not effectively treat such conditions. Any such off-label use of our product candidates could harm our reputation in the marketplace among physicians and patients. There may also be increased risk of injury to patients if physicians attempt to use our product candidates for these uses for which they are not approved, which could lead to product liability suits that might require significant financial and management resources and that could harm our reputation.

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

Currently, federal agencies in the U.S. are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA or other government agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. 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 employees and stop critical activities. If a prolonged government shutdown occurs, including as a result of reaching the debt ceiling, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

EU drug marketing and reimbursement regulations 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 both the United States and in selected foreign jurisdictions. 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 European Union, the pricing of 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. 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 healthcare reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to reward improper performance generally is typically governed by the national anti-bribery laws of EU Member States and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the European Union.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual 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, fines or imprisonment.

In addition, in some foreign countries, including some countries in the European Union, the proposed pricing for a product must be approved before it may be lawfully marketed. The requirements governing product pricing and reimbursement vary widely from country to country. For example, some EU Member States have the option to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. 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 trial 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 biotechnology products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union 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 and the potential profitability of any of our product candidates in those countries would be negatively affected.

We are subject to export and import controls, economic sanctions, and anti-corruption laws and regulations of the United States and other jurisdictions. We can face criminal liability and other serious consequences for violations of these laws and regulations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control. Export controls and trade sanctions laws and regulations may restrict or prohibit altogether the provision, sale, or supply of our products to certain governments, persons, entities, countries, and territories, including those that are the target of comprehensive sanctions or an embargo. We are also subject to anti-corruption and anti-bribery laws, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, and other state and national anti-bribery laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

If we or any third-party manufacturer we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could have a material adverse effect on our business.

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

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not

provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

Risks Related to Our Intellectual Property

We depend on in-licensed intellectual property. If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to the Janssen License, which is a non-exclusive, fully paid up, and royalty-free intellectual property license agreement. In connection with our efforts to expand our pipeline of product candidates, we expect to enter into additional license agreements in the future. We have certain obligations under the Janssen License and expect that future license agreements may impose various diligence, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licensed intellectual property, or to pursue other remedies.

We may not be able to obtain licenses at a reasonable cost or on reasonable terms, or at all. Furthermore, if we lose intellectual property rights licensed under existing agreements or fail to obtain future licenses, we may be required to expend considerable time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected proprietary technologies and product candidates, which could harm our business significantly.

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment that are important to our business. If we or our licensors do not adequately protect our or our licensors' intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. We and our licensors seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates that are important to our business. We may in the future also license or purchase patent applications filed by others. If we or our licensors are unable to secure or maintain patent protection with respect to our product candidates and any proprietary product candidates and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed.

If the scope of the patent protection we or our licensors obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing products and technology similar or identical to our product candidates or otherwise maintain a competitive advantage. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our or our licensors' patents have, or that any of our or our licensors' pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. In addition, to the extent that we license intellectual property, we cannot make assurances that those licenses will remain in force.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. The scope of the invention claimed in a patent application can be significantly reduced before the patent is issued, and this scope

can be reinterpreted after issuance. Any patents that eventually issue may be challenged, narrowed or invalidated by third parties. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by valid and enforceable patent rights. Our competitors or other third parties may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The patent prosecution process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering product candidates that we license from third parties and are reliant on our licensors. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. 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, at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our product candidates or which effectively prevent others from commercializing competitive products.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We or our licensors may in the future, become subject to a third-party pre-issuance submission of prior art, opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceeding and other similar proceedings challenging our patent rights or the patent rights of others in the U.S. Patent and Trademark Office (the "USPTO") or other foreign patent office. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our product candidates.

Furthermore, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to our product candidates.

In addition, we rely on certain of our licensors to prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them and may continue to do so in the future. We have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights or defend certain of the intellectual property that is licensed to us. It is possible that any licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

Moreover, some of our owned and in-licensed patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

If our efforts to protect the proprietary nature of the intellectual property related to our product candidates are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our product candidates. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. We, or any partners, collaborators, or licensors, 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 or our licensors' 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 partners, collaborators, or licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our 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.

We anticipate additional patent applications will be filed both in the United States and in other countries, as appropriate. However, we cannot predict:

•if additional patent applications covering new technologies related to our product candidates will be filed;

•if and when patents will issue;

•the degree and range of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;

•whether any of our intellectual property will provide any competitive advantage;

•whether any of our patents that may be issued may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;

•whether or not others will obtain patents claiming aspects similar to those covered by our or our licensors' patents and patent applications; or

•whether we or our licensors will need to initiate or defend litigation or administrative proceedings which may be costly regardless of whether we or our licensors win or lose.

Additionally, we cannot be certain that the claims in our pending patent applications covering our product candidates and their methods of use will be considered patentable by the USPTO, or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid or patentable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. These types of patents do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may, but not necessarily, contribute to a finding of infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

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

We cannot be certain that an allowed patent application will become an issued patent because there may be events that cause withdrawal of the allowance of a patent application. For example, after a patent application has been allowed, but prior to being issued, material that could be relevant to patentability may be identified. In such circumstances, the applicant may pull the application from allowance in order for the USPTO to review the application in view of the new material. We cannot be certain that the USPTO will issue the application in view of the new material. Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign countries may require the payment of maintenance fees or patent annuities during the lifetime of a patent application and/or any subsequent patent that issues from the application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar

provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application. Such noncompliance can result in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. Such an event could have a material adverse effect on our business.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering our product candidates, the defendant could counterclaim that the patent covering our product candidates, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are various grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions (such as opposition proceedings). Such proceedings could result in revocation or amendment to our or our licensors' patents in such a way that they no longer cover our product candidates. 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, our patent counsel, our licensors and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our or our licensors' rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

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

As is the case with other biotechnology and biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and biopharmaceutical industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. Obtaining and enforcing patents in the biotechnology and biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Recent patent reform legislation in the U.S. and other countries, including the Leahy-Smith America Invents Act (the "Leahy-Smith Act"), signed into law on September 16, 2011, could increase those uncertainties and costs. 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. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first-to-file" system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

Moreover, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our or our licensors' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our or our licensors' ability to obtain new patents or to enforce our or our licensors' existing patents and patents that we or our licensors might obtain in the future. We cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our or our licensors' patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce our patent rights.

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

We may not be able to pursue patent coverage of our product candidates in certain countries outside of the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may 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. The breadth and strength of our or our licensors' patents issued in foreign jurisdictions or regions may not be the same as the corresponding patents issued in the United States. Consequently, we may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the United States, 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 technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to certain territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protections, particularly those relating to biotechnology and biopharmaceutical products. This difficulty with enforcing patents could make it difficult for us to stop the infringement of our or our licensors' patents or marketing of competing products otherwise generally in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, put our or our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

Depending upon the timing, duration and specifics of any FDA marketing approval of our current product candidates, one or more of our or our licensors' U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply for a patent extension within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we believe we are entitled to, our competitors may obtain approval of competing products sooner than we would expect, and our business, financial condition, results of operations, and prospects could be materially harmed.

Third parties may initiate legal proceedings alleging that we are infringing or otherwise misappropriating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to commercialize, develop, manufacture, market, and sell our product candidates without infringing the proprietary rights of third parties. We have yet to conduct comprehensive freedom to operate searches to determine whether we would infringe patents issued to third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates, including interference proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our product candidates. 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. We could be forced, including by court order, to cease commercializing the infringing product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

•infringement and other intellectual property misappropriation which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;

•substantial damages for infringement or misappropriation, which we may have to pay if a court decides that the product or technology at issue infringes on or violates the third-party's rights, and, if the court finds we have willfully infringed intellectual property rights, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

•an injunction prohibiting us from manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party agrees to license its patent rights to us;

•even if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights protecting our product candidates; and

•we may be forced to try to redesign our product candidates or processes so they do not infringe third-party intellectual property rights, an undertaking which may not be possible or which may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue. There may be currently pending patent applications which may later result in issued patents that may be infringed by our product candidates. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents, held now or obtained in the future by a third party, were found by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product or methods use of the product, the holders of any such patents may be able to block our ability to commercialize the product unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover any aspect of our formulations, any combination therapies or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize our product candidates.

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

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming.

In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors' is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. Defense against these assertions, non-infringement, invalidity or unenforceability regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

Post-grant proceedings provoked by third parties or brought by the USPTO may be brought to determine the validity or priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or post-grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as those within the United States.

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 this type of litigation. In addition, our licensors may have rights to file and prosecute such claims, and we are reliant on them.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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

We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time-consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own.

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

In addition to seeking patents for some of our product candidates, we also rely on trade secrets, including unpatented know-how, technology, and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets,

in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We may be subject to claims that we wrongfully hired an employee from a competitor or that our employees have misappropriated intellectual property, including trade secrets of their former employers.

Many of our employees were previously employed at, or may have previously provided or may be currently providing consulting services to, universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees do not use the proprietary information or know how of others in their work for us, we may be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these employees have, inadvertently or otherwise, used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer or competitor. 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 or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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 trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

European patents and patent applications could be challenged in the recently created Unified Patent Court for the European Union.

Our or our licensors' European patents and patent applications could be challenged in the recently created Unified Patent Court ("UPC") for the European Union. We may decide to opt out our European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that our or our licensors' European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC. Under the UPC, a granted European patent would be valid and enforceable in numerous European countries. A successful invalidity challenge to a European patent under the UPC would result in loss of patent protection in those European countries. Accordingly, a single proceeding under the UPC could result in the partial or complete loss of patent protection in numerous European countries, rather than in each validated European country separately as such patents always have been adjudicated. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.

Risks Related to Ownership of Our Common Stock

An active trading market for our common stock may not be sustained.

An active or liquid market in our common stock may not be sustained. The lack of an active market may impair the value of our stockholders' shares, and our stockholders' ability to sell their shares at the desired time and price. An inactive market may also impair our ability to raise capital by selling our common stock and our ability to enter into strategic collaborations or acquire other companies, products, or technologies by using our common stock as consideration.

The price of our common stock may be volatile, which could result in substantial losses for our stockholders.

The trading price of our common stock may be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this section, these factors include:

- the commencement, enrollment, completion or results of our current or future preclinical and clinical trials for our product candidates;
- any delay in identifying and advancing a clinical candidate for our other programs;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results or delays, suspensions or terminations in future preclinical studies or clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates or the failure of a regulatory authority to accept data from preclinical studies or clinical trials conducted in other countries;
- changes in laws or regulations applicable to our product candidates, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to commercialize our product candidates, if approved;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to any of our current or future product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or product candidates in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- changes in the structure of the healthcare payment systems;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;

•trading volume of our common stock;

•changes in accounting practices;

•ineffectiveness of our internal controls;

•disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

•significant lawsuits, including patent or stockholder litigation;

•general political and economic conditions; and

•other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biotechnology and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs, reputational harm and a diversion of management's attention and resources.

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

Our quarterly and annual operating results may fluctuate significantly, due to a variety of factors, many of which are outside of our control and may be difficult to predict, including:

•the timing and cost of, and level of investment in, research, development and, if approved, commercialization activities relating to our current and future product candidates, which may change from time to time;

•the timing and status of enrollment for clinical trials;

•the cost of manufacturing our product candidates, as well as building out our supply chain, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;

•expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;

•timing and amount of any milestone, royalty or other payments due under any collaboration or license agreement, including the Janssen License;

•future accounting pronouncements or changes in our accounting policies;

•the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;

•the timing of receipt of approvals for our product candidates from regulatory authorities in the United States and internationally;

•exchange rate fluctuations;

•coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our products; and

•the level of demand for our product candidates, if approved, which may vary significantly over time.

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

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

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. Similarly, if one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Our executive officers, directors, principal stockholders and their respective affiliates own a significant percentage of our common stock and have the ability to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates collectively own a significant percentage of our outstanding common stock. As a result, these stockholders, if acting together, have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, amendment of our organizational documents, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. In addition, certain of our principal stockholders, including Third Rock Ventures V, L.P. and ARCH Venture Fund XII, L.P., have designated certain members of our board of directors. The interests of these stockholders may not be the same as or may even conflict with the interests of our other stockholders. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

Our common stock price could decline as a result of sales of a large number of shares of common stock or the perception that these sales could occur, which might also make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate.

As of December 31, 2024, we had 36,580,202 shares of common stock outstanding. Shares of unvested restricted common stock will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market stand-off or lock-up agreements. All shares of common stock sold in our initial public offering or otherwise outstanding as of our initial public offering are able to be sold in the public market. Shares issued upon the exercise of stock options pursuant to future awards that may be granted under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act of 1933, as amended (the "Securities Act").

Certain holders of our common stock have rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, until such shares can otherwise be sold without restriction under Rule 144 under the Securities Act or until the rights terminate pursuant to the terms of the stockholder agreements between us and such holders. We have registered the offer and sale of all shares of common stock that we may issue under our equity compensation plans, and those shares are available for sale in the open market, unless such shares are subject to vesting restrictions with us or lock-up restrictions. Once we register the offer and sale of shares for the holders of registration rights, they can be freely sold in the public market upon issuance, subject to the lock-up agreements.

In addition, in the future, we may issue additional shares of common stock, or other equity or debt securities convertible into common stock, in connection with a financing, acquisition, employee arrangement, or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause the price of our common stock to decline.

Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

We expect to issue additional capital stock in the future that will result in dilution to all other stockholders. Additionally, as of December 31, 2024, 6,852,229 shares of our common stock were reserved for issuance upon exercise of outstanding stock options, vested restricted stock units and performance based stock units. We expect to grant equity awards to employees, directors and consultants under our stock incentive plans. We may also raise capital through equity financings in the future. As part of our business strategy, we may acquire or make investments in complementary companies, products or technologies and issue equity securities to pay for any such acquisition or investment. Any such issuances of additional capital stock may cause stockholders to experience significant dilution of their ownership interests and the per share value of our common stock to decline.

We do not currently intend to pay dividends on our common stock and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation of the value of our common stock.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support operations and to finance the growth and development of our business. We do not intend to declare or pay any cash dividends on our capital stock in the foreseeable future. As a result, any investment return on our common stock will depend upon increases in the value for our common stock, which is not certain.

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

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

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of not less than two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our third amended and restated certificate of incorporation or amended and restated bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law (the "DGCL"), which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our amended and restated bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of, or a claim based on, fiduciary duty owed by any of our current or former directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our third amended and restated certificate of incorporation or our amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision does not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act or the Exchange Act (the "Federal Forum Provision"). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court and other state courts have upheld the validity of federal forum selection provisions purporting to require claims under the Securities Act or Exchange Act be brought in federal court, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the U.S. may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

We may not be able to continue to satisfy the listing requirements of The Nasdaq Stock Market ("Nasdaq").

We must meet certain financial and liquidity criteria to maintain our common stock's listing on Nasdaq. If we fail to meet any of Nasdaq's listing standards, our common stock may be delisted. In addition, our board of directors may determine that the cost of maintaining our listing on a national securities exchange outweighs the benefits of such listing. A delisting of our common stock from Nasdaq may materially impair our stockholders' ability to buy and sell our common stock and could have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock. The delisting of our common stock could significantly impair our ability to raise capital and the value of our stockholders' investment.

Other General Risks

Unfavorable global economic conditions, political instability and geopolitical events could adversely affect our business, financial condition, stock price, and results of operations.

Our business could be adversely affected by unstable economic and political conditions within the United States and foreign jurisdictions, including as a result of an economic downturn and geopolitical events, such as changes in the U.S. federal policy that affect the geopolitical landscape. The global credit and financial markets have also generally experienced extreme volatility and disruptions (including as a result of actual or perceived changes in interest rates, inflation and macroeconomic uncertainties), which has included severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, high inflation, uncertainty about economic stability, global supply chain disruptions, and increases in unemployment rates. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A severe or prolonged economic downturn could result in a variety of risks to our business, including a decrease in the demand for our drug candidates and in our ability to raise additional capital when needed on acceptable terms, if at all.

The financial markets and the global economy may also be adversely affected by the current or anticipated impact of political uncertainty, including military conflicts, such as the ongoing conflicts between Russia and Ukraine, and Israel and

Hamas, terrorism, or other geopolitical events. Sanctions imposed by the U.S. and other countries in response to such conflicts, including the one in Ukraine, may also continue to adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. Additionally, changes to policy implemented by the U.S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U.S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U.S. regulatory environment, inflation and other areas. For example, during the prior Trump administration, increased tariffs were implemented on goods imported into the U.S., particularly from China, Canada, and Mexico. On February 1, 2025, the U.S. imposed a 25% tariff on imports from Canada and Mexico, which were subsequently suspended for a period of one month, and a 10% additional tariff on imports from China. Historically, tariffs have led to increased trade and political tensions, between not only the U.S. and China, but also between the U.S. and other countries in the international community. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. There has also been proposed U.S. legislation that may restrict the ability of U.S. biotechnology companies to purchase services or products from, or otherwise collaborate with, certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise receive funding from, the U.S. government. We continue to assess the legislation as it develops to determine whether it could have an effect on our contractual relationships. Any changes in political, trade, regulatory, and economic conditions, including U.S. trade policies, could have a material adverse effect on our financial condition or results of operations. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.

Furthermore, any disruptions to our supply chain as a result of unfavorable global economic conditions, including due to geopolitical conflicts or public health crises, could negatively impact the timely execution of our ongoing and future clinical trials. In addition, current inflationary trends in the global economy may impact salaries and wages, costs of goods and transportation expenses, among other things, and recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures may create market and economic instability. We cannot anticipate all of the ways in which the foregoing, and the current economic climate and financial market conditions generally, could adversely impact our business.

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

Natural disasters or public health crises could severely disrupt our operations, and have a material adverse impact on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, public health crisis or other event occurred that prevented us from conducting our clinical trials, releasing clinical trial results or delaying our ability to obtain regulatory approval for our product candidates, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time.

We are eligible to be treated as an "emerging growth company" and a "smaller reporting company" and our election of 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 Jumpstart Our Business Startups Act ("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 not being required to comply with the auditor attestation requirements of Section 404, 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 stockholder approval of any golden parachute payments not previously approved. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements. We could be an emerging growth company until as late as December 31, 2029, although circumstances could cause us to lose that status earlier, including if we are deemed to be a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30, or if we have total annual gross revenue of $1.235 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404;

•providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "*Management's Discussion and Analysis of Financial Condition and Results of Operations*" disclosure;

•reduced disclosure obligations regarding executive compensation; and

•exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

Even after we no longer qualify as an emerging growth company, we could still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will 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 share price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can also take advantage of an extended transition period for complying with new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards, 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.

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 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 common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

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

As a public company, we incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements, including requiring establishment and maintenance of effective disclosure and financial reporting controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the "Dodd-Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to five years after completion of a company's IPO. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies have substantially increased, and will continue to increase, our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have an adverse effect on our business. These increased costs will continue to decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, these rules and regulations 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 the same or similar 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.

If we fail to establish and maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be reevaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which requires an annual management assessment of the effectiveness of our internal control over financial reporting. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an emerging growth company or a non-accelerated filer, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We could remain an emerging growth company until as late as December 31, 2029. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

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

We are subject to the periodic reporting requirements of the Exchange Act. We must design our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make a required related party transaction disclosure. 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.

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

As of December 31, 2024, we had approximately $13.7 million of federal net operating losses ("NOLs"). Federal NOLs generated in taxable years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOL carryforwards in a taxable year is limited to 80% of our taxable income in such year. As of December 31, 2024, we had approximately $12.0 million of state NOLs. Of the state NOLs, some are of indefinite life, but most expire at various dates, beginning in 2043. As of December 31, 2024, we had approximately $3.8 million of federal research and development tax credit carryforwards. Federal tax credit carryforwards expire at various dates, beginning in 2042. As of December 31, 2024, we had approximately $1.6 million of state research and development tax credit carryforwards. The state tax credits, which have various carryforward rules, begin to expire in 2037.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (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 "5 percent shareholders" over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. A corporation that experiences an ownership change will generally be subject to an annual limitation on the use of its pre-ownership change NOLs equal to the value of the corporation immediately before the ownership change, multiplied by the long-term tax-exempt rate (subject to certain adjustments). We may have experienced ownership changes in the past and may experience ownership changes in the future. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs by federal or state taxing authorities or other unforeseen reasons, portions of our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities. As a result, our ability to use our pre-change NOLs and tax credits to offset future taxable

income, if any, or taxes could be subject to limitations. Similar provisions of state tax law may also apply. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and tax credits.

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

U.S. federal, state, local and foreign tax laws, regulations and administrative guidance are subject to change as a result of the legislative process and review and interpretation by the U.S. Internal Revenue Service, the U.S. Treasury Department and other taxing authorities. Changes to tax laws (which changes may have retroactive application), including with respect to net operating losses and research and development tax credits, could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

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

We face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in clinical trials, and we will face an even greater risk if we commercially sell any products that we develop. While we currently have no products that have been approved for commercial sale, the ongoing, planned and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trials;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we currently hold clinical trial liability insurance, we will need to obtain and maintain additional insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to obtain and maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

We may become involved in litigation that could divert management's attention and harm our business, and insurance coverage may not be sufficient to cover all costs and damages.

From time to time we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal data, contractual relations with collaborators and licensors and intellectual property rights. In the past, securities class action litigation has often followed certain significant business transactions, such as the sale of a company or announcement of any other strategic transaction, the announcement of negative events, such as negative results from clinical trials, or periods of volatility in the market price of a company's securities. These events may also result in or be concurrent with investigations by the SEC. We may be exposed to such litigation or investigation even if no wrongdoing occurred. Litigation and investigations are usually expensive and divert management's attention and resources, which could adversely affect our business and cash resources and our ability to consummate a potential strategic transaction or the ultimate value our stockholders receive in any such transaction.

Item 1B. Unresolved Staff Comments.

None

Item 1C. Cybersecurity.

Cyber Risk Management and Strategy

We have adopted cybersecurity risk management processes, in accordance with our risk profile and business size, that are designed to identify, assess, and mitigate risks from current and emerging cybersecurity threats. Our cybersecurity processes, which are informed by the National Institute of Standards and Technology Cybersecurity Framework ("NIST CSF"), are supported by a third-party Managed Service Provider ("MSP") that assists us in managing our information technology systems.

We implement a multi-layered approach to cybersecurity that includes, but is not limited to, employee security awareness training, phishing simulations, incident response planning, and various cybersecurity tools and technologies. We leverage the support of third-party information technology and security providers to manage our information technology systems, including through the performance of system scans and threat intelligence analysis. We have also previously conducted a cybersecurity risk assessment that was intended to take into account the evolving cyber threat landscape and industry best practices, and we are adapting our cyber risk strategy in an effort to mitigate emerging cybersecurity risks.

We maintain a risk-based process to assess and review the cybersecurity practices of our third-party vendors, as appropriate, based on the level of access which the vendor has to critical operations, our information technology systems, and personally identifiable information.

To date, we have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition; however, like other companies in our industry, we have, from time to time, experienced threats and cybersecurity incidents relating to our information technology systems and infrastructure. Our third party vendors may also experience threats and cybersecurity incidents from time to time. For more information, please refer to Item 1A, "Risk Factors," in this annual report on Form 10-K.

Governance Related to Cybersecurity Risk

Management is responsible for identifying, considering and assessing material risks for the business, including risks related to cybersecurity, on an ongoing basis. Our Chief Information Officer ("CIO") is responsible for our overall IT strategy and operations, including the strategic direction of our cybersecurity program, cybersecurity risk oversight and monitoring of the prevention, detection, mitigation, and remediation of cybersecurity incidents. The individual serving as our CIO has over 10 years of experience in information security.

Our Board of Directors has delegated oversight of our cybersecurity risk management program to our Audit Committee, per the Audit Committee Charter. Our CIO provides quarterly updates to the Audit Committee regarding our cybersecurity risks and an annual enterprise risk management update, which includes updates on plans intended to enhance our overall cybersecurity posture, to the Audit Committee. The Audit Committee updates the full Board of Directors on matters relating to cybersecurity risk management as needed.

Item 2. Properties

Our corporate headquarters are located in Boston, Massachusetts, where we lease and occupy approximately 11,000 square feet of office space. Our Boston lease expires in December 2026. We will continue to occupy this space in Boston until the commencement of our sublease of a larger space in Boston, comprised of approximately 15,000 square feet of office space which is expected to commence in June 2025 and will expire in November 2031.

We also lease and occupy approximately 21,000 square feet of office and laboratory space in San Diego, California. We relocated to this space from our prior office and laboratory space in San Diego, California in January 2025. Our new San Diego, California lease will expire in December 2029.

We believe our current and future facilities in Boston and San Diego are sufficient for our needs for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations, cash flows and prospects because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Our common stock has been publicly traded on the Nasdaq Global Market under the symbol "RAPP" since June 7, 2024. Prior to this date, there was no public market for our common stock.

Holders

As of February 28, 2025, there were approximately 50 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividends

We have never declared or paid cash dividends on our capital stock. We do not anticipate declaring or paying, in the foreseeable future, any cash dividends on our capital stock. We intend to retain all available funds and future earnings, if any, to fund the development and expansion of our business. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to applicable laws, and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects, and other factors our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by this item is incorporated herein by reference to Part III, Item 12 of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

None.

Issuer Repurchases of Equity Securities

None.

Use of Proceeds from Initial Public Offering and Concurrent Private Placement

On June 6, 2024, our Registration Statement on Form S-1 (No. 333-279486) relating to our initial public offering ("IPO") was declared effective by the U.S. Securities and Exchange Commission (the "SEC"). Concurrently with the IPO, we also completed a private placement in which we issued and sold an aggregate of 1,058,824 shares of our common stock at the IPO price. There has been no material change in the planned use of proceeds from our IPO and concurrent private placement as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended, on June 7, 2024.

Item 6. Reserved

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

*You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and related notes and other financial information included elsewhere in this Annual Report on Form 10-K (this "Annual Report"). This discussion and analysis and other parts of this Annual Report contain forward-looking statements based upon our current plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, strategies, objectives, expectations, intentions and beliefs. Our actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under "*Risk Factors*" and elsewhere in this Annual Report. You should carefully read the "Risk Factors" section of this Annual Report to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see "Special Note Regarding Forward-Looking Statements." Our historical results are not necessarily indicative of the results that may be expected for any period in the future.*

Overview

We are a clinical-stage biotechnology company dedicated to discovering and developing small molecule precision medicines for patients with neurological or psychiatric disorders. Our foundational science has elucidated complexities of neuronal receptor biology and enables us to map and target certain neuronal receptor complexes. Neuronal receptors are complex assemblies of proteins, comprising receptor principal subunits and their receptor associated proteins ("RAPs"), the latter of which play crucial roles in regulating receptor expression and function. We believe that our deep expertise in RAP biology provides an opportunity for us to interrogate previously inaccessible targets and develop neurological and psychiatric drugs that are specific for receptor variants and neuroanatomical regions associated with certain diseases. Most neuroactive drugs lack this specificity, often resulting in undesired and intolerable side effects. Leveraging our expertise, we are developing a portfolio of precision product candidates that we believe has the potential to transform the standard of care of many neurological and psychiatric disorders.

Our founders have made pioneering discoveries related to the function of RAPs in the brain. Their findings form the basis of our RAP technology platform, which enables a differentiated approach to generate precision small molecule product candidates with the potential to overcome many limitations of conventional neurology drug discovery. RAP-219, our most advanced product candidate, is an AMPA receptor ("AMPAR") negative allosteric modulator ("NAM"). RAP-219 is designed to achieve neuroanatomical specificity through its selective targeting of a RAP known as TARPγ8, which is associated with the neuronal AMPARs. Whereas AMPARs are distributed widely in the central nervous system ("CNS"), TARPγ8 is expressed only in discrete regions, including the hippocampus and neocortex, where focal seizures often originate. By contrast, TARPγ8 has minimal expression in the hindbrain, where drug effects are often associated with adverse events. As such, we believe RAP-219 has the potential for a differentiated profile as compared to traditional neuroscience medications. Due to the role of AMPA biology in various neurological disorders and our precision approach of selectively targeting TARPγ8, we believe RAP-219 has pipeline-in-a-product potential and we are evaluating it as a potentially transformational treatment for patients with focal epilepsy, bipolar disorder, and peripheral neuropathic pain.

A total of four Phase 1 trials in RAP-219 have been conducted to date in healthy adult volunteers: a single ascending dose ("SAD") trial; a multiple ascending dose ("MAD") trial; a second MAD trial ("MAD-2"), to assess dosing regimens that may accelerate time to reach therapeutic exposure; and a human positron emission tomography ("PET") trial, which utilized a companion PET radiotracer to confirm brain target receptor occupancy and brain region specificity across a range of dosing and exposure levels. In January 2025, we announced results from our PET and MAD-2 trials of RAP-219. Data demonstrated that neuroanatomical specificity can be achieved through RAP-219's selective targeting of TARPγ8. In Cohort 1 of the human PET trial, which used the dosing regimen utilized in our ongoing Phase 2a trial in patients with refractory focal epilepsy, RAP-219 achieved target receptor occupancy associated with maximal seizure protection in preclinical models within five days and was generally well tolerated, which we believe further supports the use of such dosing regimen in the Phase 2a trial in patients with refractory focal epilepsy.

We are currently conducting a Phase 2a proof-of-concept trial in adult patients with refractory focal epilepsy, for which we expect to report topline results in the third quarter of 2025. We believe RAP-219 also has therapeutic potential in bipolar disorder and peripheral neuropathic pain, and we intend to initiate a Phase 2a proof-of-concept trial in bipolar mania in the third quarter of 2025 with topline results expected in the first half of 2027. We were notified in the fourth quarter of 2024 by the U.S. Food and Drug Administration ("FDA") that the Investigational New Drug ("IND") submitted for the initiation of a Phase 2a proof-of-concept trial of RAP-219 for the treatment of diabetic peripheral neuropathic pain ("DPNP") was placed on clinical hold. The FDA requested additional information and amendments specific to the protocol design. The clinical hold is specific to the IND for DPNP and has not impacted our ongoing Phase 2a trial in refractory focal epilepsy or planned proof-of-concept trial in bipolar

mania. We believe in our ability to advance the clinical development of RAP-219 for DPNP and will provide an update on the anticipated timing of the Phase 2a trial initiation once available.

Beyond TARPγ8, we have two advanced discovery-stage nicotinic acetylcholine receptor ("nAChR") programs stemming from our RAP technology platform. The first comprises modulators of α6 nAChRs that we are developing in chronic pain; and the second comprises modulators of α9α10 nAChRs that we are developing in hearing disorders. Third-party genetic data suggest that these nAChR subtypes could be attractive drug targets for these diseases. We continue to leverage our RAP technology platform to discover additional product candidates that we believe have the potential to provide a transformative benefit for large patient populations with neurological or psychiatric diseases with unmet needs.

Since our inception in February 2022, we have not generated any revenue from product sales or other sources and have incurred significant operating losses and negative cash flows from our operations. We have devoted substantially all of our efforts to organizing and staffing our company, business planning, research and development activities, building our intellectual property portfolio, and providing general and administrative support for these operations. In June 2024, we completed our initial public offering ("IPO"), pursuant to which we issued and sold 9,200,000 shares of common stock (inclusive of 1,200,000 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares). In addition, we issued and sold 1,058,824 shares of common stock to certain institutional accredited investors in a concurrent private placement. The aggregate net proceeds received by us from the IPO and concurrent private placement were $157.6 million, after deducting underwriting discounts and commissions, placement agent fees as well as other offering and private placement costs of $16.8 million. To date, we have funded our operations primarily with proceeds from the issuance and sale of our common stock, convertible notes and convertible preferred stock. As of December 31, 2024, we had raised aggregate gross proceeds of $424.4 million from these financings, and had cash, cash equivalents and short-term investments of $305.3 million, excluding our restricted cash.

We have incurred significant operating losses in each year since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of any product candidates we may develop. Our net losses were $78.3 million and $34.8 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $123.7 million. We expect our expenses and operating losses will increase substantially as we:

- continue to conduct our ongoing clinical trials of RAP-219, including advancement into late-stage global clinical trials, as well as initiate and complete additional clinical trials of future product candidates or current product candidates in new indications or patient populations;
- conduct our ongoing preclinical studies and ongoing and planned clinical trials;
- utilize third parties to manufacture our potential future product candidates and related raw materials;
- continue our early research and development activities;
- seek to identify additional research programs and program candidates to expand our pipeline;
- hire additional research and development, clinical, commercial, and operational personnel;
- maintain, expand, enforce, defend and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek regulatory approvals for any potential future product candidates for which we successfully complete clinical trials;
- acquire or in-license product candidates, intellectual property and technologies;
- establish and maintain collaborations;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any therapies for which we may obtain regulatory approval; and
- incur additional costs associated with being a public company, including audit, legal, regulatory, and tax-related services associated with maintaining compliance with an exchange listing and Securities Exchange Commission ("SEC") requirements, director and officer insurance premiums and investor relations costs.

In addition, we have several preclinical and clinical development, regulatory, and commercial milestone payment obligations under our licensing arrangements. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year,

depending on the timing of our preclinical studies and planned clinical trials and our expenditures on other research and development activities.

We do not expect to generate any revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our potential future product candidates, which will not be for at least the next several years, if ever. If we obtain regulatory approval for any of our potential future product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, until such time as we can generate significant revenue from sales of our potential future product candidates, if ever, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. See the section titled "*—Liquidity and Capital Resources*" included elsewhere in this Annual Report. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market potential future product candidates that we would otherwise prefer to develop and market ourselves.

We believe that our existing cash and cash equivalents, and short-term investments will enable us to fund our operating expenses and capital expenditure requirements through the end of 2026. See the sections titled "*—Liquidity and Capital Resources" and "Risk Factors—Risks Related to Our Limited Operating History, Financial Condition and Need for Additional Capital*" included elsewhere in this Annual Report.

License and Collaboration Agreements

Option and License Agreement with Janssen Pharmaceutical NV

In August 2022, we entered into an option and license agreement with Janssen Pharmaceutical NV, as amended on April 3, 2023, April 18, 2023, May 2, 2023, October 2, 2023, and April 9, 2024 (collectively, the "Janssen License"), under which we received an exclusive option to obtain from Janssen (a) a worldwide exclusive license for the research, development, and commercialization of transmembrane TARPγ8 AMPAR products for the diagnosis, treatment, prophylaxis or palliation of any disease or condition in humans or other animals (the "Field") and (b) an assignment of certain patents related to TARPγ8, in each case of (a)-(b), subject to certain retained rights by Janssen. Pursuant to the Janssen License, we also received a worldwide, royalty-free, non-exclusive license (exclusive under certain joint patents) for the research, development, and commercialization of certain neuronal nicotinic acetylcholine ("nACh") products in the Field.

We made a non-refundable, non-creditable upfront payment of $1.0 million to Janssen after we entered into the Janssen License. In October 2022, we exercised the option and paid a non-refundable, non-creditable option fee of $4.0 million to Janssen. If we succeed in developing and commercializing TARPγ8 products, Janssen will be eligible to receive (i) up to $76.0 million in development milestone payments and up to $40.0 million sales milestone payments for the product containing the lead TARPγ8 development candidate, and (ii) up to $25.0 million in development milestone payments and up to $42.0 million sales milestone payments for other TARPγ8 products containing a non-lead TARPγ8 development candidate.

Janssen is also eligible to receive (a) royalties ranging from mid to high-single digit percentages on worldwide net sales of any products containing a TARPγ8 development candidate and (b) royalties ranging from low to mid-single digit percentages for other TARPγ8 products that do not contain a TARPγ8 development candidate, in each case of (a) and (b), subject to potential reductions following the expiration of valid claims and regulatory exclusivity covering such TARPγ8 products, the launch of certain generic products and the application of certain anti-stacking reductions for third party intellectual property payments, subject to a customary reduction floor. The royalties for any TARPγ8 product will expire on a country-by-country basis upon the latest to occur of (i) the expiration of all valid patent claims covering such product in such country, (ii) the expiration of all regulatory exclusivities in such country, and (iii) a specified number of years following the first commercial sale of such product in such country. The Janssen License provides us with certain other exclusive rights with respect to small molecules with activity against TARPγ8 and nACh.

We have the right to terminate the Janssen License for any or no reason upon providing prior written notice to Janssen upon ninety (90) days' prior written notice to Janssen. Either party may terminate the license agreement in its entirety for the other party's material breach if such party fails to cure the breach or upon certain insolvency events involving the other party.

NeuroPace Master Services Agreement and Statement of Work

In November 2023, we entered into a master services agreement (the "NeuroPace Agreement") with NeuroPace Inc. ("NeuroPace"), the manufacturer and distributor of the responsive neurostimulation ("RNS") system. Pursuant to the NeuroPace Agreement and in accordance with statement of work agreements entered into from time to time, NeuroPace provides us with certain services with respect to data from the RNS systems used in our clinical trials. The NeuroPace Agreement also grants us a royalty-free, worldwide, exclusive, non-transferable license to all data collected by the RNS systems in our Phase 2a clinical trial and the outcomes of algorithms that are applied to such data, as well as the ability to publish the outcomes of algorithms, subject to certain conditions. The consideration we will pay to NeuroPace for such services is set out in each statement of work agreement.

The NeuroPace Agreement contains an exclusivity provision providing that, at any time while providing services under the NeuroPace Agreement and for a period after the final clinical study report, NeuroPace may not perform any services that are the same as the services covered by the NeuroPace Agreement to any business that directly competes with us, subject to the specific terms of the NeuroPace Agreement. The NeuroPace Agreement also contains standard representations and warranties, confidentiality and intellectual property protective provisions and indemnification terms.

The NeuroPace Agreement expires on the later of three years from the effective date or the completion of all services under all statement of work agreements entered into prior to the third anniversary of the effective date. Either party may terminate the NeuroPace Agreement or any statement of work agreement (i) without cause by giving written notice to the other party within a specified period of time, (ii) by giving written notice upon a curable material breach that is not remediated within a specified period of time, or (iii) immediately upon written notice in the event of a material breach that cannot be cured.

Concurrently with the execution of the NeuroPace Agreement, the parties also entered into an initial statement of work, as amended in March 2024 (the "NeuroPace SOW"), under the NeuroPace Agreement, pursuant to which NeuroPace agreed to provide services related to our Phase 2a clinical trial of RAP-219, including, among other things, clinical trial readiness support, identification of potential patients satisfying the enrollment criteria and RNS system data reporting and data analysis. Pursuant to the payment schedule set out in the NeuroPace SOW, we will pay NeuroPace an aggregate of up to $3.7 million over a period of approximately two years in connection with NeuroPace's provision of services and achievement of certain patient enrollment and deliverable milestones.

During the year ended December 31, 2024, we paid NeuroPace $0.6 million and recognized $1.8 million in research and development expense for services performed, resulting in a prepaid expense balance of $0.3 million as of December 31, 2024. During the year ended December 31, 2023, we paid NeuroPace $1.5 million, which was recorded as prepaid expenses and other current assets in the consolidated balance sheet as of December 31, 2023.

Components of Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the development and research of our clinical and pre-clinical potential future product candidates. Our research and development expenses include:

- personnel-related costs, including salaries, bonuses, benefits, and stock-based compensation for employees engaged in manufacturing, research and development functions;
- the costs to acquire in-process research and development with no alternative future use acquired in an asset acquisition;
- external expenses, including expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, consultants and our clinical and scientific advisors;
- the cost of developing and validating our outsourced manufacturing process for use in our preclinical studies and future clinical trials;
- the cost to obtain licenses to intellectual property and related future payments should certain development milestones be achieved;
- costs for laboratory supplies, research materials, and reagents; and

•facility costs, depreciation, and other expenses related to research and development activities, which include direct or allocated expenses for rent, maintenance of facilities, and utilities.

Our primary focus since inception has been the development of RAP-219. Our research and development costs consist primarily of personnel-related costs and external costs, such as fees paid to Contract Manufacturing Organizations ("CMOs"), Contract Research Organizations ("CROs") and consultants in connection with our non-clinical studies, preclinical studies and clinical trials. We expense all research and development costs in the periods in which they are incurred. Because we are working on multiple research and development programs at one time, we track many of our external expenses on a program-by-program basis. We do not allocate personnel-related costs or other indirect costs, to specific product development programs because these costs are deployed across multiple programs and, as such, are not separately classified.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher and more variable development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in the near term as we advance RAP-219 through clinical development, pursue regulatory approval of RAP-219, continue to discover and develop additional product candidates and incur expenses associated with hiring additional personnel to support our research and development efforts, including the associated manufacturing activities.

Upfront and milestone payments made are accrued for and expensed when the achievement of the milestone is probable up to the point of regulatory approval. Milestone payments made upon regulatory approval will be capitalized and amortized over the remaining useful life of the related product.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

•the timing and progress of preclinical and clinical development activities;

•timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;

•effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any product candidates we may develop;

•successful enrollment and completion of clinical trials, including under the U.S. FDA's current Good Clinical Practices ("GCPs"), current Good Laboratory Practices ("GLPs"), and any additional regulatory requirements from foreign regulatory authorities;

•positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;

•receipt of marketing approvals from applicable regulatory authorities;

•establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;

•establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any product candidates we may develop; and

•maintenance of a continued acceptable safety, tolerability and efficacy profile of any product candidates we may develop following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates or potential future product candidate could mean a significant change in the costs and timing associated with the development of that product candidate or potential future product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate would be required for the completion of clinical development of a product candidate or potential future product candidate, or if we experience significant delays in our clinical trials due to slower than expected patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development. We may never obtain regulatory approval for any of our product candidates, and, even if we do, drug commercialization takes several years and millions of dollars in development costs.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, bonuses, benefits, and stock-based compensation charges for those individuals in executive, finance, human resources, facility operations, and other administrative functions. Other costs include legal fees relating to intellectual property and corporate matters, professional fees for auditing, accounting, tax and consulting services, office and information technology costs, insurance costs, and facilities, depreciation and other general and administrative expenses, which include direct or allocated expenses for rent and maintenance of facilities and utilities.

We anticipate that our general and administrative expenses will increase for the foreseeable future to support development of product candidates and our continued research activities. These increases will likely include additional costs related to the hiring of additional personnel and fees paid to outside consultants, among other expenses. We also anticipate increased expenses related to audit, accounting, legal, regulatory, and tax-related services associated with maintaining compliance with The Nasdaq Global Market ("Nasdaq") and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Other Income (Expense)

Interest Income

Interest income consists of interest earned from our cash, cash equivalents and short-term investments.

Change in Fair Value of Preferred Stock Tranche Right Liabilities

Our Series A and Series B convertible preferred stock purchase agreements provided the investors the obligation to participate in subsequent offerings of Series A and Series B convertible preferred stock upon achievement of certain specified milestones, upon the waiver of such milestone achievement by a majority vote of the respective series convertible preferred stockholders, or with respect to the Series B convertible preferred stock, upon exercise of the stockholders right to early exercise the preferred stock tranche right. The preferred stock tranche rights are classified as liabilities and initially recorded at fair value upon the issuance date of the rights. The liabilities were subsequently remeasured to fair value at each reporting date and immediately prior to being settled, and changes in fair value of the preferred stock tranche right liabilities were recognized as a component of other income (expense), net in our consolidated statements of operations and comprehensive loss. In February 2023, we closed the Series A second and third financings, resulting in full settlement of the tranche right, upon both of which we issued additional shares of Series A convertible preferred stock. Immediately prior to the issuance of such shares, the preferred stock tranche right liability was remeasured to fair value with the change in fair value recognized as a component of other income (expense), net. As a result of the Series A preferred stock tranche right settlement in February 2023, we will no longer recognize changes in the fair value of the Series A preferred stock tranche liability in our consolidated statements of operations and comprehensive loss. In March 2024, we closed the Series B second financing, resulting in full settlement of the tranche right, upon which we issued additional shares of Series B convertible preferred stock. Immediately prior to the issuance of such shares, the preferred stock tranche right liability was remeasured to fair value with the change in fair value recognized as a component of other income (expense), net. As a result of the Series B preferred stock tranche right settlement in March 2024, we will no longer recognize changes in the fair value of the Series B preferred stock tranche liability in our consolidated statements of operations and comprehensive loss.

Income Taxes

For the years ended December 31, 2024 and 2023, we recorded an income tax provision of zero and $10 thousand, respectively. As of December 31, 2024 and 2023, we recorded a full valuation allowance of our net deferred tax assets, as we believed it was more likely than not we would not be able to utilize our deferred tax assets prior to their expiration.

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each year or for our research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating losses ("NOLs"), carryforwards and tax credits will be not realized. As of December 31, 2024, we had federal NOL carryforwards of approximately $13.7 million and state NOL carryforwards of approximately $12.0 million, respectively. Federal losses have an indefinite carryforward period, but can only offset 80% of federal taxable income in a given year. Losses for state purposes begin to expire in 2043. As of December 31, 2024, we also had federal and state tax research and development credit carryforwards of approximately $3.8 million and $1.6 million, respectively, to offset future tax liabilities,

which begin to expire in 2042 and 2037, respectively. We have recorded a full valuation allowance against our net deferred tax assets at December 31, 2024. As of December 31, 2024, we had no unrecognized tax benefits.

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:

	For the year ended December 31, 2024	2023	Change
	(in thousands)		
Operating expenses			
Research and development	$ 60,935	$ 27,999	$ 32,936
General and administrative	22,120	8,180	13,940
Total operating expenses	83,055	36,179	46,876
Loss from operations	(83,055)	(36,179)	(46,876)
Other income (expense):			
Interest income	12,138	2,527	9,611
Change in fair value of preferred stock tranche right liability	(7,390)	(1,124)	(6,266)
Total other income (expense), net	4,748	1,403	3,345
Net loss before income taxes	(78,307)	(34,776)	(43,531)
Provision for income taxes	—	10	(10)
Net loss	$ (78,307)	$ (34,786)	$ (43,521)

Operating Expenses

Research and Development Expenses

	For the year ended December 31, 2024	2023	Change
	(in thousands)		
Direct external program expenses:			
RAP-219 program	$ 22,080	$ 10,202	$ 11,878
Preclinical programs	16,535	6,335	10,200
Internal and unallocated expenses:			
Personnel-related costs (including stock-based compensation)	19,500	9,939	9,561
Other costs	2,820	1,523	1,297
Total research and development expenses	$ 60,935	$ 27,999	$ 32,936

Research and development expenses were $60.9 million for the year ended December 31, 2024, as compared to $28.0 million for the year ended December 31, 2023. The increase of $32.9 million consisted of the following:

- an $11.9 million increase in RAP-219 program costs, which consisted primarily of an increase of $7.4 million in clinical trial costs primarily driven by costs for our Phase 2a trial in refractory focal epilepsy, start-up costs for our Phase 2a proof-of-concept trial in DPNP, costs from our MAD-2 trial, costs from our PET trial, and costs from our human absorption, distribution, metabolism, and excretion study, a $1.7 million increase in preclinical toxicology studies driven by initiation of long-term toxicology work, a $2.4 million increase in contract manufacturing costs related to the production of materials to support our additional Phase 1 and 2 trials, and an increase of $0.2 million for consulting related to the DPNP program;

- a $10.2 million increase in preclinical program costs, which consisted primarily of a $6.0 million increase in toxicology and animal studies related to our discovery programs, a $1.9 million increase in external chemistry efforts related to our discovery programs, a $1.0 million increase in contract manufacturing costs related to the production of materials for use in our preclinical studies, a $1.2 million increase in lab supply costs due to increased preclinical activities, and a $0.2 million increase in discovery program consulting costs;

•a $9.6 million increase in personnel-related costs due to an increase in headcount, which consisted primarily of salaries, bonuses, and other compensation-related costs of $7.7 million, and stock-based compensation of $2.2 million. These increases were partially offset by a decrease in general research and development consulting costs of $0.3 million; and

•a $1.3 million increase in other costs, consisting of research and development facilities expenses and depreciation expense related to opening our Boston office in September 2023, and continuing to expand our San Diego site.

General and Administrative Expenses

	For the year ended December 31,		
	2024	2023	Change
	(in thousands)		
Personnel-related (including stock-based compensation)	$ 13,989	$ 4,324	$ 9,665
Professional and consulting costs	5,482	3,158	2,324
Facility related and other	2,649	698	1,951
Total general and administrative expense	$ 22,120	$ 8,180	$ 13,940

General and administrative expense were $22.1 million for the year ended December 31, 2024, as compared to $8.2 million for the year ended December 31, 2023. The increase of $13.9 million consisted of the following:

•$9.7 million increase in workforce expense due to an increase in headcount, consisting of salaries, bonuses, and other compensation-related costs of $5.1 million and stock-based compensation of $4.6 million;

•$2.3 million increase in professional and consulting fees, related to expanding our administrative support to satisfy the requirements of operating as a public company along with the general growth of the Company, including outsourced legal and accounting expenses; and

•$1.9 million increase in other expenses, consisting primarily of administrative expenses due to increased business activities, and expanded general and administrative support in connection with operating as a public company.

Other Income (Expense)

	For the year ended December 31,		
	2024	2023	Change
	(in thousands)		
Other income (expense):			
Interest income	$ 12,138	$ 2,527	$ 9,611
Change in fair value of preferred stock tranche right liability	(7,390)	(1,124)	(6,266)
Total other income (expense), net	$ 4,748	$ 1,403	$ 3,345

Interest Income

Interest income was $12.1 million for the year ended December 31, 2024, as compared to $2.5 million for the year ended December 31, 2023. The increase of $9.6 million is primarily due to opening additional interest-bearing accounts in December 2023, in addition to the increased cash, cash equivalent and short-term investments balances from the Series B convertible preferred stock financing in August 2023 and February 2024, and our initial public offering ("IPO") in June 2024.

Change in Fair Value of Preferred Stock Tranche Right Liability

The change in fair value of the preferred stock tranche right liability expense was $7.4 million for the year ended December 31, 2024, as compared to $1.1 million for the year ended December 31, 2023 . The change in fair value of preferred stock tranche right liabilities for the year ended December 31, 2024 consisted of an increase in the fair value of the Series B preferred stock tranche right liability of $7.4 million. In conjunction with the waiver of the second tranche milestone in February 2024 and the settlement of the Series B tranche right in March 2024, the Series B tranche right liability was remeasured immediately prior to the waiver, resulting in a $7.4 million increase in fair value. The change in fair value of preferred stock tranche right liability for the year ended December 31, 2023 consisted of an increase in the fair value of the Series A preferred

stock tranche right liability of $1.0 million as a result of the waiver of the second and third milestones and settlement of the Series A tranche right liability.

Income Taxes

For the years ended December 31, 2024 and 2023 we recorded an income tax provision of zero and $10 thousand, respectively.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception in February 2022, we have not generated any revenue from any sources and have incurred significant operating losses and negative cash flows from operations. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidates and pipeline. Further, we expect to continue to incur additional costs associated with operating as a public company. To date, we have funded our operations with proceeds from the sale of convertible notes, convertible preferred stock, and the issuance of common stock in our IPO and concurrent private placement. Through December 31, 2024, we received aggregate gross proceeds of $424.4 million from the issuance of convertible promissory notes and the sale of our convertible preferred stock and common stock. As of December 31, 2024, we had cash and cash equivalents of $56.8 million and short-term investments of $248.5 million.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	For the year ended December 31,	
	2024	2023
	(in thousands)	
Net cash used in operating activities	$ (64,828)	$ (27,181)
Net cash used in investing activities	(170,141)	(78,860)
Net cash provided by financing activities	221,625	145,136
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (13,344)	$ 39,095

Operating Activities

During the year ended December 31, 2024 operating activities used $64.8 million of cash, resulting primarily from our net loss of $78.3 million, non-cash accretion of investments in marketable securities of $3.2 million, and changes in operating assets and liabilities of $2.4 million, partially offset by $10.2 million of non-cash stock-based compensation expense, non-cash change in fair value of preferred stock tranche right liability of $7.4 million, $0.8 million of non-cash depreciation expense, and $0.6 million of non-cash lease expense. The $2.4 million change in operating assets and liabilities is primarily driven by an increase in prepaid expenses and other current assets of $1.9 million, primarily due to advanced payments on new contracts related to our clinical trials, an increase in accrued expenses of $0.4 million and decrease in accounts payable of $0.3 million and due to payments to vendors, and $0.7 million decrease in operating lease liabilities.

During the year ended December 31, 2023, operating activities used $27.2 million of cash, resulting primarily from our net loss of $34.8 million, partially offset by $3.5 million of non-cash stock-based compensation expense and non-cash change in fair value of preferred stock tranche right liability of $1.1 million, and net cash provided by changes in operating assets and liabilities of $2.7 million. Net cash provided by changes in operating assets and liabilities consisted primarily of increases in accrued expenses and other current liabilities of $5.4 million, partially offset by increases in prepaid expenses and other current assets of $3.2 million. The increases in accrued expenses and prepaid expenses were primarily due to increased internal and external costs associated with our research and development activities, including clinical trials and manufacturing.

Investing Activities

During the year ended December 31, 2024, net cash used in investing activities was $170.1 million, primarily consisting of purchases of short-term investments of $377.5 million and purchases of property and equipment of $2.4 million, partially offset by maturities of short-term investments of $209.8 million.

During the year ended December 31, 2023, net cash used in investing activities was $78.9 million, primarily consisting of purchases of short-term investments of $77.2 million and purchases of property and equipment of $1.6 million.

Financing Activities

During the year ended December 31, 2024, net cash provided by financing activities was $221.6 million, primarily consisting of net proceeds from our IPO and concurrent private placement of our common stock in the aggregate amount of $157.7 million, and net proceeds of $63.9 million from our additional issuance of Series B convertible preferred stock.

During the year ended December 31, 2023, net cash provided by financing activities was $145.1 million, primarily consisting of net proceeds of $59.9 million from our additional issuance of Series A convertible preferred stock, and net proceeds of $85.3 million from our initial issuance of Series B convertible preferred stock, including tranche rights.

Future Funding Requirements

As of December 31, 2024, we had cash, cash equivalents and short-term investments of $305.3 million, excluding our restricted cash. As of the issuance date of the consolidated financial statements for the year ended December 31, 2024, we expect that our cash, cash equivalents and short-term investments will be sufficient to fund our operating expenses and capital expenditure requirements through at least 12 months from the issuance of the consolidated financial statements. We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements through the end of 2026. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. However, our forecast for 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. Additionally, the process of conducting preclinical studies and testing potential future product candidates in clinical trials is costly, and the timing of progress and expenses in these studies and trials is uncertain. We will need to raise substantial additional capital in the future.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our preclinical studies and the current and future clinical trials of our product candidates. Our funding requirements and timing and amount of our operating expenditures will depend on many factors, including:

- the rate of progress in the development of RAP-219 and our other product candidates;
- the type, number, scope, progress, expansions, results, costs, and timing of, discovery efforts, preclinical studies and clinical trials of RAP-219 and potential future product candidates;
- the costs and timing of manufacturing for RAP-219 and our potential future product candidates and commercial manufacturing;
- the costs, timing, and outcome of regulatory review of our product candidates;
- the terms and timing of establishing and maintaining licenses and other similar arrangements;
- the legal costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company;
- the costs associated with hiring additional personnel and consultants as our preclinical and future clinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any potential future product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- costs associated with any products or technologies that we may in-license or acquire; and
- costs associated with being a public company.

Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, potentially including collaborations, licenses, and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when

needed on favorable terms or at all. 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 the rights of our common stockholders. Additional debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise funds through collaborations, license arrangements, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or potential future product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. Our failure to raise capital or enter into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional funds through equity or debt financings, or through other sources when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates and potential future product candidates even if we would otherwise prefer to develop and market such potential future product candidates ourselves.

Contractual Obligations and Commitments

Leases

As of the December 31, 2024, we had future minimum operating lease payments under non-cancelable leases of $1.8 million related to leases we have recognized on our consolidated balance sheet, which are due over the following 2.5 years. In addition, we have one lease in San Diego that has been entered into but has not yet commenced, for which we expect to pay approximately $9.6 million over the five-year lease term. We also entered into a sublease agreement for a facility in Boston, for which we expect to pay approximately $5.2 million over the six and a half-year sublease term.

Option and License Agreement with Janssen Pharmaceutical NV

We made an upfront non-refundable, non-creditable payment of $1.0 million to Janssen after we entered into the Janssen License. In October 2022, we exercised the option and made a non-refundable, non-creditable option fee of $4.0 million to Janssen. If we succeed in developing and commercializing TARPγ8 products, Janssen will be eligible to receive (i) up to $76.0 million in development milestone payments and up to $40.0 million sales milestone payments for the product containing the lead TARPγ8 development candidate and (ii) up to $25.0 million in development milestone payments and up to $42.0 million sales milestone payments for the other products containing a non-lead TARPγ8 development candidate. We are also required to pay tiered royalties related to the TARPγ8 development candidate of a mid to high single-digit percentage on worldwide net sales and tiered royalties related to the TARPγ8 products that do not contain a TARPγ8 development candidate of low to mid single-digit percentages on annual net sales of the products covered by the license.

NeuroPace Master Services Agreement and Statement of Work

In connection with the execution of the NeuroPace Agreement, the parties also entered into an initial statement of work under the NeuroPace Agreement, pursuant to which NeuroPace agreed to provide services related to our Phase 2a proof-of-concept clinical trial of RAP-219, including, among other things, clinical trial readiness support, data analysis and data reporting. Pursuant to the payment schedule set out in the statement of work, we will pay NeuroPace an aggregate of up to $3.7 million over a period of approximately two years in connection with NeuroPace's provision of services and achievement of certain patient enrollment and deliverable milestones.

During the year ended December 31, 2023, we paid NeuroPace $1.5 million, which was recorded as prepaid expenses and other current assets in the consolidated balance sheet as of December 31, 2023. During the year ended December 31, 2024, we paid NeuroPace $0.6 million and recognized $1.8 million in research and development expense for services performed, resulting in a prepaid expense balance of $0.3 million as of December 31, 2024.

Apart from the contracts with payment commitments that we have documented above, we have entered into contracts in the normal course of business with CROs, CMOs and other third parties for preclinical research studies and testing, clinical trials and manufacturing services. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice and, as a result, are not included in the table of contractual obligations and commitments above. Payments due upon cancellation consist only of payments for services provided and expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation.

Critical Accounting Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States ("GAAP"). The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported amounts of expenses incurred during the reporting periods. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and expenses that are not readily apparent from other sources. We evaluate our estimates and judgments on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in Note 2—*"Summary of Significant Accounting Policies"* to our annual consolidated financial statements, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Research and Development Expenses and Accruals

We expense research and development expenses as incurred. Research and development expenses represent costs incurred by us for the discovery and development of our product candidates and include employee salaries and benefits, including stock-based compensation, third-party research and development expenses, including amounts incurred under agreements with our external vendors and consultants engaged to perform preclinical and clinical studies, contract manufacturing and research services, consulting costs, laboratory supplies, and certain allocated expenses, as well as amounts incurred under third-party license agreements.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. We estimate preclinical study and clinical trial and other research and development expenses based on the services performed, pursuant to contracts with research institutions and third-party service providers that conduct and manage preclinical studies and clinical trials and research services on our behalf. We record the costs of research and development activities based upon the estimated services provided but not yet invoiced and include these costs in accrued expenses and other current liabilities in our consolidated balance sheets and in research and development expense in our consolidated statements of operations and comprehensive loss. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from external third-party service providers. Contingent milestone payments, if any, are expensed when the milestone results are probable and estimable, which is generally upon the achievement of the milestone.

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services provided and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that may be used to conduct and manage clinical trials on our behalf. We generally accrue expenses related to clinical trials based on contracted amounts applied to the level of patient enrollment and activity. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

Stock-Based Compensation

We measure stock-based awards granted to employees, directors, and nonemployees based on their fair value on the date of the grant. We recognize compensation expense for awards to employees and directors over the requisite service period, which is generally the vesting period of the respective award. Compensation expense for awards to non-employees with service-based vesting conditions is recognized in the same manner as if we had paid cash in exchange for the goods or services, which is generally over the vesting period of the award. For stock-based awards with service-based vesting conditions, we recognize compensation expense using the straight-line method. For stock-based awards with performance-based vesting conditions, we recognize compensation expense using the graded-vesting method over the requisite service period using the accelerated attribution method, commencing when achievement of the performance condition becomes probable. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. For awards to

non-employees, the expected term of the option is equal to the contractual term of the non-employees' service agreement. The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of our common stock on that same date.

Determination of the Fair Value of Common Stock

As there had been no public market for our common stock prior to June 2024, the estimated fair value of our common stock had been determined by our board of directors as of the date of each option grant 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. Our common stock valuation was prepared using either the option-pricing method ("OPM") or the hybrid method, both of which used a market approach to estimate our enterprise value. The OPM treats common stock and convertible preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the convertible preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. The hybrid method is a probability-weighted expected return method ("PWERM") where the equity value in one or more of the scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for us, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock.

These third-party valuations were performed at various dates, which resulted in valuation of our common stock of $11.57 per share as of March 31, 2024. Our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of convertible preferred stock and the superior rights and preferences of the convertible preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of clinical and preclinical studies for our product candidates;
- our stage of development and our business strategy;
- external market conditions affecting the biotechnology and biopharmaceutical industries and trends within these industries;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our convertible preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering ("IPO") or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biotechnology industry.

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

Following our IPO, in connection with our accounting for granted stock options and other awards we may grant, the fair value of our common stock is determined based on the quoted market price of our common stock.

Valuation of Preferred Stock Tranche Liability

Our Series A and Series B convertible preferred stock purchase agreements obligated the Series A and Series B investors to participate in a subsequent offering of Series A and Series B convertible preferred stock upon certain conditions being met, which we referred to as the preferred stock tranche rights. We determined that the preferred stock tranche rights were required to be recorded as liabilities because they were freestanding financial instruments that would require us to transfer assets upon exercises of the right. The preferred stock tranche rights met the definition of a freestanding financial instrument because they were legally detachable and separately exercisable from the Series A and Series B convertible preferred stock. The preferred stock tranche rights were classified as a liability and initially recorded at fair value upon the issuance date of the right. The liabilities were remeasured to fair value at each reporting date until settled, and changes in the fair value of the preferred stock tranche right liabilities were recognized as a component of other income (expense) in our consolidated statements of operations and comprehensive loss.

In February 2023, in conjunction with the amendment to the Series A convertible preferred stock purchase agreement, our existing Series A convertible preferred stockholders voted to waive the second and third tranche milestones and exercised their tranche right. As a result, an aggregate of 50,000,000 shares of Series A convertible preferred stock were issued and sold at a price of $1.00 per share, resulting in total cash proceeds of $50 million, less $61 thousand of issuance costs. As a result of this issuance, the Series A preferred stock tranche right liability, with a then fair value of $11.5 million immediately prior to the amendment and waiver, was settled in full and recognized in additional paid-in capital.

In August 2023 and concurrent with the original issuance of the Series B convertible preferred stock, two stockholders exercised their right to early exercise the Series B preferred stock tranche right and purchased 10,731,725 shares. Consequently, we recognized $1.2 million in additional paid-in capital associated with the simultaneous original issuance and early exercise. Additionally, the investors paid a premium of $1.7 million for these shares over their fair value which was also recorded in additional paid-in capital.

Subsequent to the original issuance, one stockholder exercised its right to early exercise the Series B preferred stock tranche right and purchased 4,769,655 shares of Series B convertible preferred stock for cash proceeds of $8.0 million. The fair value of the associated tranche right liability that was settled at the time of the sale of $0.5 million was recognized in additional paid-in capital. Additionally, the investor paid a premium of $0.8 million for these shares over their fair value which was also recorded in additional paid-in capital.

In February 2024, our Series B convertible preferred stockholders voted to waive the second tranche milestones and purchase the remaining Series B milestone tranche shares. Immediately prior to the waiver, we remeasured the Series B tranche right liability to be $11.6 million and recognized $7.4 million in other expense for the change in the fair value of the Series B tranche right liability during the period. As a result of the waiver, we remeasured the Series B tranche right liability to be $4.2 million and recognized the change in fair value of $7.4 million in additional paid-in capital as a capital contribution. In conjunction with the closing that occurred in March 2024, an aggregate of 38,157,240 shares of Series B convertible preferred stock were issued at a price of $1.67727 per share, resulting in total cash proceeds of $64.0 million, less $87 thousand of issuance costs. As a result of this issuance, the Series B preferred stock tranche right liability with a then fair value of $4.2 million was settled in full and recognized as part of the carrying value of the Series B convertible preferred stock.

The fair value of the tranche right liabilities was determined based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy. The fair value of the tranche right liabilities was determined using a Contingent Forward Analysis, which is a scenario-based lattice model that accounts for the different possible milestone scenarios and their associated probabilities, as estimated by us. The valuation model considered the probability of closing the tranche, the estimated future value of the convertible preferred stock to be issued at each closing and the investment required at each closing. Future values were converted to present value using a discount rate appropriate for probability-adjusted cash flows. The most significant assumptions in the Contingent Forward Analysis impacting the fair value of the preferred stock tranche rights were the fair value of the Series A and Series B convertible preferred stock as of each remeasurement date, the estimated remaining term of the tranche right as of each remeasurement date, and the probabilities of success for each tranche milestone as of each measurement date. We determined the fair value per share of the underlying convertible preferred stock by taking into consideration the most recent sales of our convertible preferred stock as well as additional factors that we deemed relevant. We assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. The risk-free rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining estimated time to each tranche closing.

As of December 31, 2023, the fair value of each Series B convertible preferred stock was $1.68 per share. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining estimated time period of achievement of the specified milestones underlying the preferred stock tranche right. As of December 31, 2023, an immediate 10 percent increase in the fair value of our Series B convertible preferred stock would have resulted in a

$0.9 million increase, and in the case of a 10 percent decrease, a $0.9 million decrease to the fair value of the preferred stock tranche right liability.

The fair value of each share of Series B convertible preferred stock was estimated to be $1.79 per share on February 26, 2024 and March 19, 2024.

Emerging Growth Company and Smaller Reporting Company Status

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company. As a result of this election, our consolidated financial statements may not be comparable to other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

Recent Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2—"*Summary of Significant Accounting Policies*" to our consolidated financial statements included elsewhere in this Annual Report.

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

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

Item 8. Financial Statements and Supplementary Data.

Rapport Therapeutics, Inc.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Rapport Therapeutics, Inc.

Opinion on the Financial Statements

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

Basis for Opinion

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

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

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

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 11, 2025

We have served as the Company's auditor since 2023.

Rapport Therapeutics, Inc.
Consolidated Balance Sheets
(In thousands, except share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets		
Cash and cash equivalents	$ 56,805	$ 70,169
Short-term investments	248,475	77,309
Restricted cash	105	85
Prepaid expenses and other current assets	4,417	3,309
Total current assets	309,802	150,872
Property and equipment, net	3,529	1,916
Operating lease right of use asset, net	1,442	2,084
Other assets	160	551
Total assets	$ 314,933	$ 155,423
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities		
Accounts payable [(1)]	$ 1,954	$ 2,502
Accrued expenses and other current liabilities [(1)]	6,076	5,631
Operating lease liability	737	670
Total current liabilities	8,767	8,803
Series B preferred stock tranche right liability	—	4,200
Operating lease liability, net of current portion	739	1,476
Total liabilities	9,506	14,479
Commitments and contingencies (Note 13)		
Series A convertible preferred stock, $0.001 par value; zero and 100,182,354 shares authorized as of December 31, 2024 and 2023, respectively; zero shares and 100,182,354 shares issued and outstanding as of December 31, 2024 and 2023, respectively; liquidation preference of zero and $100,182 as of December 31, 2024 and 2023, respectively	—	89,487
Series B convertible preferred stock, $0.001 par value; zero and 89,431,030 shares authorized as of December 31, 2024 and 2023, respectively; zero and 51,273,790 shares issued and outstanding as of December 31, 2024 and 2023, respectively; liquidation preference of zero and $86,000 as of December 31, 2024 and 2023, respectively	—	77,091
Stockholders' equity (deficit)		
Undesignated preferred stock, $0.001 par value; 10,000,000 shares and zero shares authorized at December 31, 2024 and 2023, respectively; zero shares issued and outstanding at both December 31, 2024 and 2023	—	—
Common stock, $0.001 par value; 500,000,000 shares and 250,000,000 shares authorized at December 31, 2024 and 2023, respectively; 36,580,202 shares and 4,170,817 shares issued and outstanding as of December 31, 2024 and 2023, respectively	37	4
Additional paid-in capital	429,657	19,796
Accumulated other comprehensive income (loss)	(522)	4
Accumulated deficit	(123,745)	(45,438)
Total stockholders' equity (deficit)	305,427	(25,634)
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	$ 314,933	$ 155,423

(1)Includes related party amounts of zero and $0.2 million (accounts payable) and zero (accrued expenses) as of both December 31, 2024 and 2023, respectively (see Notes 5 and 10).

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

Rapport Therapeutics, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	For The Year Ended December 31,	
	2024	2023
Operating expenses		
Research and development [1]	$ 60,935	$ 27,999
General and administrative [2]	22,120	8,180
Total operating expenses	83,055	36,179
Loss from operations	(83,055)	(36,179)
Other income (expense):		
Interest income	12,138	2,527
Change in fair value of preferred stock tranche right liability	(7,390)	(1,124)
Total other income, net	4,748	1,403
Net loss before income taxes	(78,307)	(34,776)
Provision for income taxes	—	10
Net loss	$ (78,307)	$ (34,786)
Net loss per share attributable to common stockholders, basic and diluted	$ (3.78)	$ (23.10)
Weighted-average common shares outstanding, basic and diluted	20,738,338	1,505,774
Comprehensive loss:		
Net loss	$ (78,307)	$ (34,786)
Change in unrealized gains (losses) on investments, net of tax	(526)	4
Total other comprehensive income (loss)	(526)	4
Comprehensive loss	$ (78,833)	$ (34,782)

(1)Includes related party amounts of less than $0.1 million and $0.7 million for the years ended December 31, 2024 and 2023, respectively (see Note 10).
(2)Includes related party amounts of $0.1 million and $0.9 million for the years ended December 31, 2024 and 2023, respectively (see Note 10).

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

Rapport Therapeutics, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated Other Comprehensive Income	Accumulated	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	(Loss)	Deficit	(Deficit)
Balance at December 31, 2022	40,182,354	$ 29,567	—	$ —	3,587,345	$ 4	$ 586	$ —	$ (10,652)	$ (10,062)
Issuance of Series A convertible preferred stock for the settlement of the second and third tranche right liability, net of issuance costs of $80	60,000,000	59,920	—	—	—	—	11,465	—	—	11,465
Issuance of Series B convertible preferred stock, net of Series B preferred stock tranche right liability of $4,619 and issuance costs of $632	—	—	46,504,135	69,860	—	—	2,887	—	—	2,887
Issuance of Series B convertible preferred stock for the settlement of the second tranche right liability	—	—	4,769,655	7,231	—	—	1,283	—	—	1,283
Issuance of restricted common stock	—	—	—	—	630,174	1	53	—	—	54
Repurchase of unvested restricted common stock	—	—	—	—	(46,702)	—	(4)	—	—	(4)
Stock-based compensation expense	—	—	—	—	—	—	3,525	—	—	3,525
Net loss	—	—	—	—	—	—	—	—	(34,786)	(34,786)
Change in unrealized gain on investments, net of tax	—	—	—	—	—	—	—	4	—	4
Balance at December 31, 2023	100,182,354	$ 89,487	51,273,790	$ 77,091	4,170,817	$ 4	$ 19,796	$ 4	$ (45,438)	$ (25,634)
Issuance of Series B convertible preferred stock for the settlement of the tranche right liability, net of issuance costs of $87	—	—	38,157,240	68,161	—	—	7,343	—	—	7,343
Conversion of Series A convertible preferred stock to common stock upon closing of the initial public offering	(100,182,354)	(89,487)	—	—	11,701,298	12	89,475	—	—	89,487
Conversion of Series B convertible preferred stock to common stock upon closing of the initial public offering	—	—	(89,431,030)	(145,252)	10,445,518	10	145,242	—	—	145,252
Issuance of common stock from initial public offering, net of issuance costs of $15,519	—	—	—	—	9,200,000	9	140,859	—	—	140,868
Issuance of common stock from private placement, net of issuance cost of $1,297	—	—	—	—	1,058,824	1	16,701	—	—	16,702
Issuance of common stock upon exercise of stock options	—	—	—	—	3,745	1	6	—	—	7
Stock-based compensation expense	—	—	—	—	—	—	10,235	—	—	10,235
Net loss	—	—	—	—	—	—	—	—	(78,307)	(78,307)
Change in unrealized gain (loss) on investments, net of tax	—	—	—	—	—	—	—	(526)	—	(526)
Balance at December 31, 2024	—	$ —	—	$ —	36,580,202	$ 37	$ 429,657	$ (522)	$ (123,745)	$ 305,427

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

Rapport Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	For the year ended December 31, 2024	2023
Cash flows from operating activities:		
Net loss	$ (78,307)	$ (34,786)
Adjustments to reconcile net loss to net cash used in operating activities		
Non-cash interest (income) expense	—	(6)
Depreciation and amortization	839	112
Net accretion of investments in marketable securities	(3,211)	(75)
Change in fair value of preferred stock tranche right liability	7,390	1,124
Non-cash lease expense	642	206
Stock-based compensation expense	10,235	3,525
Series A and B preferred stock issuance costs allocated to tranche right liabilities	—	67
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,854)	(3,200)
Other assets	83	(240)
Accounts payable	(346)	856
Accrued expenses and other current liabilities	371	5,380
Operating lease liabilities	(670)	(144)
Net cash used in operating activities	(64,828)	(27,181)
Cash flows from investing activities		
Purchases of short-term investments	(377,532)	(77,224)
Maturities of short-term investments	209,796	—
Purchases of property and equipment	(2,405)	(1,636)
Net cash used in investing activities	(170,141)	(78,860)
Cash flows from financing activities		
Proceeds from initial public offering and concurrent private placement, net of underwriter discounts and commissions and deferred offering costs	157,705	—
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs paid	—	59,920
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs paid	63,913	85,300
Proceeds from issuance restricted common stock	—	54
Repurchase of unvested restricted common stock	—	(4)
Proceeds from exercise of stock options	7	—
Payment of deferred offering costs	—	(134)
Net cash provided by financing activities	221,625	145,136
Net (decrease) increase in cash, cash equivalents, and restricted cash	(13,344)	39,095
Cash, cash equivalents, and restricted cash at beginning of period	70,254	31,159
Cash, cash equivalents, and restricted cash at end of period	$ 56,910	$ 70,254
Supplemental disclosure for noncash investing and financing activities:		
Right-of-use assets obtained in exchange for operating lease liabilities	$ —	$ 2,290
Settlement of Series A preferred stock tranche right liability	$ —	$ 11,465
Settlement of Series B preferred stock tranche right liability	$ 11,590	$ 513
Deferred offering costs included in accounts payable and accrued expenses at period end	$ —	$ 177
Conversion of Series A convertible preferred stock into common stock upon closing of initial public offering	$ 89,487	$ —
Conversion of Series B convertible preferred stock into common stock upon closing of initial public offering	$ 145,252	$ —
Purchases of property and equipment included in accounts payable and accrued expenses at period end	$ 172	$ 123
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	$ 56,805	$ 70,169
Restricted cash	$ 105	$ 85
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	$ 56,910	$ 70,254

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

1. Nature of the Business and Basis of Presentation

Rapport Therapeutics, Inc., together with its consolidated subsidiary (the "Company") is a clinical-stage biotechnology company dedicated to discovering and developing small molecule precision medicines for patients with neurological or psychiatric disorders. The Company was incorporated in the state of Delaware in February 2022 as Precision Neuroscience NewCo, Inc. In October 2022, the Company changed its name to Rapport Therapeutics, Inc. The Company is located in Boston, Massachusetts and San Diego, California.

The Company is subject to risks and uncertainties common to early stage companies in the biotechnology industry, including, but not limited to, completing preclinical studies and clinical trials, obtaining regulatory approval for product candidates, market acceptance of products, development by competitors of new technological innovations, dependence on key personnel, the ability to attract and retain qualified employees, reliance on third-party organizations, protection of proprietary technology, compliance with government regulations, and the ability to raise additional capital to fund operations. The Company's product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure, and extensive compliance-reporting capabilities. Even if the Company's development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Reverse stock split

On May 31, 2024, the Company effected a one-for-8.5648 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios of each series of the Company's preferred stock (see Note 6). Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratio.

Liquidity

The accompanying consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. The Company has incurred recurring losses since its inception, including net losses of $78.3 million and $34.8 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, the Company had an accumulated deficit of $123.7 million. In June 2024, the Company completed its initial public offering ("IPO") and concurrent private placement of its common stock which resulted in net proceeds of $157.6 million. The Company had cash and cash equivalents and short-term investments, excluding restricted cash, of $305.3 million as of December 31, 2024. The Company expects to continue to generate operating losses for the foreseeable future. The Company expects that its cash and cash equivalents and short-term investments will be sufficient to fund its operating expenses and capital expenditure requirements through at least 12 months from the issuance of these consolidated financial statements.

The Company will need additional financing to support its continuing operations and pursue its growth strategy. Until such time as the Company can generate significant revenue from product sales, if ever, it expects to finance its operations though equity offerings, debt financings or other capital sources, including collaborations with other companies or other strategic transactions. The Company may not be able to obtain funding on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders.

The inability to raise capital as and when needed would have a negative impact on the Company's financial condition and its ability to pursue its business strategy. The company will need to generate significant revenue to achieve profitability, and it may never do so.

If the Company is unable to obtain funding, it could be forced to delay, reduce or eliminate some or all of its research and development programs, which could adversely affect its business prospects, or it may be unable to continue operations. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Basis of Presentation

The accompanying consolidated financial statements reflect the operations of the Company. Intercompany balances and transactions have been eliminated in consolidation. The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of the Company's consolidated 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 at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting periods. Significant estimates and assumptions reflected within these consolidated financial statements include, but are not limited to, research and development expenses and accruals, the valuation of the Company's common stock and stock-based awards and the valuation of preferred stock tranche right liability. The Company bases its estimates on known trends and other market-specific or relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates, as there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results may differ materially from those estimates or assumptions.

Concentrations of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and short-term investments. The Company maintains its cash and cash equivalents at high-quality and accredited financial institutions in amounts that could exceed federally insured limits. Cash equivalents are invested in money market funds and U.S. Treasury bills. However, the Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships. The Company's short-term investments consist of U.S. Treasury bills, government securities, and government agency securities and as a result, the Company believes represent minimal credit risk.

Restricted cash

Restricted cash at December 31, 2024 was $0.1 million, which was restricted as cash collateral for the Company's business credit card program. Restricted cash as of December 31, 2023 consisted of a letter of credit totaling $85 thousand that was established in connection with an anticipated lease arrangement, which was cancelled prior to commencement due to failure of the landlord to complete its obligations. Consequently, the letter of credit and related cash restriction were released in March 2024.

Short-term investments

The Company's short-term investments consist of investments in debt securities, including U.S. Treasury bills, government securities, and U.S. agency securities with remaining maturities beyond three months at the date of purchase that are available to be converted into cash to fund its current operations. As of December 31, 2024 and 2023, all of the Company's debt securities were classified as available-for-sale and were carried at fair market value (see Note 3). The unrealized gains and losses on the Company's available-for-sale debt securities are recorded in other comprehensive income (loss) in the consolidated statements of operations and comprehensive loss.

Debt securities in an unrealized loss position are evaluated for impairment at least quarterly. For available-for-sale debt securities in an unrealized loss position, the Company first assesses whether or not it intends to sell, or it is more likely than not that it will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the investment security's amortized cost basis is written down to fair value through net loss.

For available-for-sale debt securities that do not meet the aforementioned criteria, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors. In conducting this assessment for debt securities in an

unrealized loss position, management evaluates the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors.

If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the investment security are compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded for the credit loss, limited by the amount that the fair value is less than the amortized cost basis. Any unrealized loss that has not been recorded through an allowance for credit loss is recognized in other comprehensive income (loss). As of December 31, 2024 and 2023, there was no allowance for credit losses recorded on the Company's consolidated balance sheet.

The Company's interest income consists of interest earned from cash, cash equivalents, and short-term investments.

Deferred Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of an equity financing, these costs are recorded as a reduction of the proceeds from the offering, either as a reduction of the carrying value of the convertible preferred stock or in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the in-process equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the consolidated statements of operations and comprehensive loss. Upon closing of the Company's IPO in June 2024, these deferred offering costs were included in the $16.8 million issuance costs classified to stockholders equity (deficit) and recorded against the proceeds from the offering. As of December 31, 2024 and 2023, the Company recorded deferred offering costs of $0 million and $0.3 million, respectively, in other assets on its balance sheet.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents, short-term investments, and preferred stock tranche right liabilities are carried at fair value, determined according to the fair value hierarchy described above (see Note 3). The carrying values of the Company's accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

Asset Classification	Estimated Useful Life
Computer equipment	3 years
Lab equipment	5 years
Leasehold Improvements	Shorter of remaining lease term or useful life

Costs for capital assets not yet placed into service are capitalized and are depreciated once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance that do not improve or extend the life of the respective assets are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist primarily of property and equipment, and operating lease 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. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. If such asset group is considered to not be recoverable, the impairment loss to be recognized is measured based on the excess of the carrying value of the impaired asset group over its fair value.

For the years ended December 31, 2024 and 2023, the Company did not recognize any impairment losses on long-lived assets.

Segment Information

The Company operates and manages its business as a single segment for the purposes of assessing performance and making operating decisions. The Company's chief executive officer, who is the chief operating decision maker, reviews the Company's financial information on a consolidated basis for purposes of evaluating financial performance and allocating resources. All of the Company's long-lived assets are located in the United States (see Note 11).

Preferred Stock Tranche Right Liabilities

The purchase agreements for the Company's Convertible Preferred Stock (see Note 6) provided investors the obligation to participate in subsequent offerings of Convertible Preferred Stock and the Company an obligation to issue additional Convertible Preferred Stock, at the initial offering price, when certain conditions were met.

The Company classified the preferred stock tranche right as a liability on its consolidated balance sheet as each preferred stock tranche right was a freestanding financial instrument that may require the Company to transfer assets to settle its obligation (upon events that are outside of its control). The preferred stock tranche right liability was initially recorded at fair value upon the date of issuance and subsequently remeasured to fair value at each reporting date. Changes in the fair value of the preferred stock tranche right liability were recognized as a component of other income (expense) in the consolidated statement of operations and comprehensive loss. Any issuance costs allocated to the preferred stock tranche right liability were immediately expensed.

Research and Development Expenses

Costs for research and development activities are expensed as incurred. Research and development expenses consist of costs incurred in connection with performing research and development activities, including amounts incurred under agreements with external vendors and consultants engaged to perform preclinical and clinical studies and to manufacture research and development materials for use in such studies, salaries and related personnel costs, stock-based compensation, consultant fees, and third-party license fees.

Upfront payments under license agreements are expensed upon receipt of the license, and annual maintenance fees under license agreements are expensed over the maintenance period. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable. Contingent milestone payments, if any, are expensed when the milestone results are probable and estimable, which is generally upon the achievement of the milestone.

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

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Contingencies

The Company is subject to contingent liabilities, such as legal proceedings and claims, that arise in the ordinary course of business activities. The Company accrues for loss contingencies when losses become probable and are reasonably estimable. If the reasonable estimate of the loss is a range and no amount within the range is a better estimate, the minimum amount of the range is recorded as a liability on the consolidated balance sheets. The Company does not accrue for contingent losses that, in its judgment, are considered to be reasonably possible, but not probable; however, it discloses the range of reasonably possible losses. As of December 31, 2024 and 2023, no liabilities were recorded for loss contingencies (see Note 13).

Stock-Based Compensation

The Company measures all stock options granted to employees, directors and non-employees based on the fair value of the awards on the date of grant using the Black-Scholes option-pricing model. For awards to non-employees, the expected term of the option is equal to the contractual term of the non-employees' service agreement. The Company measured restricted stock awards using the difference, if any, between the purchase price per share of the award and the fair value of the Company's common stock at the date of grant.

The Company grants stock options and restricted stock awards that are subject to either service or performance-based vesting conditions and performance restricted stock units that are subject to performance-based vesting conditions. Compensation expense for awards to employees and directors with service-based vesting conditions is recognized using the straight-line method over the requisite service period, which is generally the vesting period of the respective award. Compensation expense for awards to non-employees with service-based vesting conditions is recognized in the same manner as if the Company had paid cash in exchange for the goods or services, which is generally over the vesting period of the award. Forfeitures are accounted for as they occur. Compensation expense for awards to employees and non-employees with service and performance-based vesting conditions is recognized based on the grant-date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. As of each reporting date, the Company estimates the probability that specified performance criteria will be met and does not recognize compensation expense until it is probable that the performance-based vesting condition will be achieved.

The Company also grants performance-based restricted stock units ("PSUs") to certain employees that are subject to performance-based vesting conditions. The PSUs will vest in two equal tranches over two performance periods starting on the grant date and ending, respectively, on December 31, 2025, and December 31, 2026, subject to the satisfaction of both service and performance conditions specifically defined for each performance period and each PSU award. The performance conditions are related to the achievement of certain program milestones in the Company's drug discovery and development process.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Leases

The Company determines if an arrangement is a lease at inception. Operating lease right-of-use ("ROU") assets and liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. As the Company's leases do not provide an implicit rate, it uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The operating lease ROU asset also includes any lease payments made and is reduced by lease incentives received. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term in general and administrative expenses. The Company classifies leases at the lease commencement date as operating or finance leases and records a right-of-use asset and a lease liability on the consolidated balance sheet for all leases with an initial lease term of greater than 12 months. Leases with an initial term of 12 months or less are not recorded in the balance sheet, but payments are recognized as expense on a straight-line basis over the lease term. The Company enters into contracts that contain both lease and non-lease components. Non-lease components may include maintenance, utilities, and other operating costs. The Company combines the lease and non-lease components of fixed costs in its lease arrangements as a single lease component. Variable costs, such as utilities or maintenance costs, are not included in the measurement of right-of-use assets and lease liabilities, but rather are expensed when the event determining the amount of variable consideration to be paid occurs.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined based on the differences between the financial statement basis and tax basis of assets and liabilities using enacted tax rates in effect for the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50 percent likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties. The Company had accrued no amounts for interest or penalties related to uncertain tax positions as of December 31, 2024 and 2023.

Net Loss Per Share

The Company calculated basic and diluted net loss per share attributable to common stockholders using the two-class method required for companies with participating securities. The Company considers Series A convertible preferred stock and Series B convertible preferred stock to be participating securities as the holders are entitled to receive cumulative dividends as well as residuals in liquidation.

Under the two-class method, basic net loss per share available to common stockholders was calculated by dividing the net loss available to common stockholder by the weighted-average number of shares of common stock outstanding during the period, which excludes unvested restricted stock. The net loss available to common stockholders was not allocated to the Series A convertible preferred stock or Series B convertible preferred stock as the holders of convertible preferred stock did not have a contractual obligation to share in losses. Diluted net loss per share available to common stockholders was computed by giving effect to all potentially dilutive common stock equivalents outstanding for the period. For purposes of this calculation, preferred stock, unvested restricted stock and stock options were considered common stock equivalents but had been excluded from the calculation of diluted net loss per share available to common stockholders as their effect was anti-dilutive. In periods in which the Company reports a net loss available to common stockholders, diluted net loss per share available to common stockholders is the same as basic net loss per share available to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Following the closing of its IPO, the Company only has one class of shares outstanding, and basic net loss per common share is computed by dividing the net loss by the weighted average number of shares of common stock outstanding for the period. Diluted net loss per common share is computed by dividing net loss by the weighted average number of shares of common stock outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock awards. For periods in which the Company reports a net loss, diluted net loss per common share is the same as basic net loss per common share, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the year ended December 31, 2024, comprehensive loss includes unrealized loss on short-term investments. For the year ended December 31, 2023, comprehensive loss includes unrealized gains on short-term investments.

Recently Adopted Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures ("ASU 2023-07"), which requires all public entities, including public entities with a single reportable segment, to provide in interim and annual periods one or more measures of segment profit or loss used by the chief operating decision maker to allocate resources and assess performance. Additionally, the standard requires disclosures of significant segment expenses and other segment items as well as incremental qualitative disclosures. The guidance in this update is effective for fiscal years beginning after December 15, 2023, and interim periods after December 15, 2024. The Company's adoption of the standard has no impact on its consolidated statement of operations and comprehensive loss or statement of cash flows.

Recently Issued Accounting Pronouncements Not Yet Adopted

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures ("ASU 2023-09"), which requires enhanced income tax disclosures, including specific categories and disaggregation of information in the effective tax rate reconciliation, disaggregated information related to income taxes paid, income or loss from continuing operations before income tax expense or benefit, and income tax expense or benefit from continuing operations. The requirements of the ASU are effective for annual periods beginning after December 15, 2024, with early adoption permitted. The Company is currently in the process of evaluating the effects of this pronouncement on its related disclosures.

In November 2024, the FASB issued ASU 2024-03, Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses, which requires disclosures about specific types of expenses included in the expense captions presented on the face of the income statement as well as disclosures about selling expenses. The requirements of the ASU are effective for annual periods beginning after December 15, 2026, and for interim periods beginning after December 15, 2027, with early adoption permitted. The requirements will be applied prospectively with the option for retrospective application. The Company is currently in the process of evaluating the effects of this pronouncement on its related disclosures.

3. Fair Value Measurements

The following tables present the Company's fair value hierarchy for its assets and liabilities that are measured at fair value on a recurring basis and indicate the level within the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value (in thousands):

	Fair Value Measurements at December 31, 2024			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 9,432	$ —	$ —	$ 9,432
Short-term investments:				
U.S. Treasury bills		28,723		28,723
Government securities		136,514		136,514
Government agency securities		83,238		83,238
	$ 9,432	$ 248,475	$ —	$ 257,907

	Fair Value Measurements at December 31, 2023			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 23,441	$ —	$ —	$ 23,441
U.S. Treasury bills	—	23,832	—	23,832
Short-term investments:				
U.S. Treasury bills and government securities	—	77,309	—	77,309
	$ 23,441	$ 101,141	$ —	$ 124,582
Liabilities				
Series B preferred stock tranche right liability	$ —	$ —	$ 4,200	$ 4,200
	$ —	$ —	$ 4,200	$ 4,200

Money market funds are highly liquid and actively traded marketable securities that generally transact at a stable $1.00 net asset value representing its estimated fair value. During the years ended December 31, 2024 and 2023, there were no transfers between Level 1, Level 2 and Level 3.

The Company classifies its marketable securities as short-term because they are available to be converted into cash to fund current operations. The fair value of the Company's U.S. Treasury bills, government securities, and government agency securities are classified as Level 2 because they are valued using observable inputs to quoted market prices, benchmark yields, reported trades, broker/dealer quotes or alternative pricing sources with reasonable levels of price transparency and U.S. Treasury securities.

The underlying securities held in the money market funds held by the Company are all government backed securities.

Short-term investments consisted of the following (in thousands):

	December 31, 2024			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Short-term investments:				
U.S. Treasury bills	$ 28,694	$ 30	$ —	$ 28,724
Government securities	136,829	—	(316)	136,513
Government agency securities	83,474	—	(236)	83,238
	$ 248,997	$ 30	$ (552)	$ 248,475

	December 31, 2023			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Short-term investments:				
U.S. Treasury bills and government securities	$ 77,305	$ 4	$ —	$ 77,309
	$ 77,305	$ 4	$ —	$ 77,309

The contractual maturities of the Company's short-term investments in available-for-sale debt securities held were as follows (in thousands):

	December 31, 2024	December 31, 2023
Due within one year	$ 117,761	$ 77,309
Due between one and two years	130,714	—
	$ 248,475	$ 77,309

As of December 31, 2024, all investments in an unrealized loss position were in this position for less than 12 months. The Company evaluated its securities for potential other-than-temporary impairment and considered the decline in market value to be

primarily attributable to current economic and market conditions. Additionally, the Company does not intend to sell the securities in an unrealized loss position and does not expect it will be required to sell the securities before recovery of the unamortized cost basis. Given the Company's intent and ability to hold such securities until recovery, and the lack of a significant change in credit risk for these investments, the Company does not consider these investments to be impaired as of December 31, 2024. The Company did not recognize any credit losses during both the years ended December 31, 2024 and 2023.

Valuation of Preferred Stock Tranche Right Liability

The Series A and Series B preferred stock tranche right liabilities in the tables above and below are composed of the fair value of obligations to issue Series A convertible preferred stock and Series B convertible preferred stock, respectively (see Note 6), either upon achievement of certain specified milestones, upon the waiver of such milestone achievement by a majority vote of the respective series convertible preferred stockholders or in relation to the Series B convertible preferred stock, upon a shareholder exercising its right to early exercise the tranche right. The fair value of the tranche right liability was determined based on significant inputs not observable in the market, which represented a Level 3 measurement within the fair value hierarchy. The fair value of the tranche right liabilities were determined using a Contingent Forward Analysis, which is a scenario-based lattice model that accounts for the different possible milestone scenarios and their associated probabilities, as estimated by the Company. The valuation model considered the probability of closing the tranche, the estimated future value of the Convertible Preferred Stock to be issued at each closing and the investment required at each closing. Future values were converted to present value using a discount rate appropriate for probability-adjusted cash flows. The risk-free rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining estimated time to each tranche closing.

Series A Preferred Stock Tranche Right Liability

The following tables provide a roll-forward of the aggregate fair value of the Company's Series A preferred stock tranche right liability during the year ended December 31, 2023, for which fair value is determined using Level 3 inputs (in thousands):

	Series A Preferred Stock Tranche Right Liability
Balance as of December 31, 2022	$ 10,435
Change in fair value of Series A preferred stock tranche right liability	1,030
Settlement of Series A preferred stock tranche right liability upon waiver of milestone	(11,465)
Balance as of December 31, 2023	$ —

Series B Preferred Stock Tranche Right Liability

The significant unobservable inputs used in the valuation model to measure the Series B preferred stock tranche right liability that is categorized within Level 3 of the fair value hierarchy as of December 31, 2023 are as follows:

	Second Tranche Milestone
Probability of meeting Series B milestone	80%
Milestone achievement date	12/31/2024
Risk-free rate	4.79%
Expected value of Series B if milestones are not met	$ 0.84

The following tables provide a roll-forward of the aggregate fair value of the Company's Series B preferred stock tranche right liability during the years ended December 31, 2024 and 2023, for which fair value is determined using Level 3 inputs (in thousands):

	Series B Preferred Stock Tranche Right Liability
Balance as of December 31, 2022	$ —
Initial fair value of Series B preferred stock tranche right liability	4,619
Settlement of Series B preferred stock tranche right liability upon early exercise	(513)
Change in fair value of Series B preferred stock tranche right liability	94
Balance as of December 31, 2023	$ 4,200
Change in fair value of Series B preferred stock tranche right liability	7,390
Settlement of Series B preferred stock tranche right liability upon waiver of milestone	(11,590)
Balance as of December 31, 2024	$ —

4. Property and Equipment, Net

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

	December 31, 2024	December 31, 2023
Lab equipment	$ 3,716	$ 1,719
Computer equipment	67	43
Leasehold improvements	281	255
Construction in process	430	26
Total property and equipment	4,494	2,043
Less: Accumulated depreciation	(965)	(127)
	$ 3,529	$ 1,916

Depreciation expense of property and equipment for the years ended December 31, 2024 and 2023 was $0.8 million and $0.1 million, respectively.

5. Accrued Expenses and Other Current Liabilities

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

	December 31, 2024	December 31, 2023
Research and development	$ 1,664	$ 2,645
Professional fees	235	459
Employee related	3,708	2,413
Accrued other	469	114
	$ 6,076	$ 5,631

6. Preferred Stock

Prior to the closing of the Company's IPO in June 2024, the Company had issued Series A convertible preferred stock and Series B convertible preferred stock.

On May 30, 2024, the Company's stockholders approved the third amended and restated certificate of incorporation, which was filed upon the closing of the IPO on June 10, 2024, and which, among other things, created 10,000,000 undesignated shares of authorized preferred stock, $0.001 par value per share.

Immediately prior to the closing of the Company's IPO on June 6, 2024, pursuant to the reverse stock split and a proportional adjustment to the existing conversion ratios of each series of the Company's preferred stock as discussed further below, all of the Company's outstanding shares of convertible preferred stock were converted into an aggregate of 22,146,816 shares of common stock.

Series A Convertible Preferred Stock and Series A Preferred Stock Tranche Right Liability

In December 2022, the Company completed its first closing of Series A convertible preferred stock and issued and sold 32,000,000 shares of Series A convertible preferred stock, at a price of $1.00 per share. Contemporaneously, investors converted their Convertible Promissory Notes for 8,182,354 shares of Series A convertible preferred stock, bringing the total number of shares of Series A convertible preferred stock issued to 40,182,354.

The purchase agreement for the Series A convertible preferred stock provided investors the obligation to purchase an additional 60,000,000 shares of Series A convertible preferred stock (the "Series A Milestone Tranches") at a price of $1.00 per share in the subsequent second and third tranche closings upon the achievement of specified second and third tranche milestones by the Company or the right to purchase additional shares upon waiving of such milestone achievement by a majority vote of Series A convertible preferred stockholders. Within 30 days prior to a Deemed Liquidation Event (see definition below), investors could also choose to early exercise their tranche right by providing the Company a written notice.

In February 2023, the Company amended the Series A convertible preferred stock purchase agreement to add an additional investor, who purchased 10,000,000 shares, at the price of $1.00 per share, resulting in cash proceeds of $10.0 million, less $19 thousand of issuance costs and to amend the total number of shares subject to the Series A Milestone Tranches from 60,000,000 to 50,000,000.

In conjunction with the amendment to the Series A convertible preferred stock purchase agreement, the Company's existing Series A convertible preferred stockholders agreed to waive the second and third tranche milestones and exercised the tranche right in February 2023. As a result, an aggregate of 50,000,000 shares of Series A convertible preferred stock were issued and sold at a price of $1.00 per share, resulting in total cash proceeds of $50 million, less $61 thousand of issuance costs. As a result of this issuance, the Series A preferred stock tranche right liability with a then fair value of $11.5 million immediately prior to the amendment and waiver, was settled in full and recognized in additional paid-in capital as a capital contribution.

Series B Convertible Preferred Stock and Series B Preferred Stock Tranche Right Liability

In August 2023, the Company issued and sold 46,504,135 shares of Series B convertible preferred stock, at a price of $1.67727 per share. The 46,504,135 shares include the 10,731,725 shares that were early exercised on the original issuance date (discussed below).

The purchase agreement for the Series B convertible preferred stock provided investors the obligation to purchase an additional 42,926,895 shares of Series B convertible preferred stock (the "Series B Milestone Tranche") at a price of $1.67727 per share in the subsequent closing upon the achievement of a specified milestone by the Company or the right to purchase additional shares upon waiving of such milestone achievement by a majority vote of Series B convertible preferred stockholders. Additionally, each stockholder of Series B convertible preferred stock had the right to early exercise the tranche right by providing three days advance written notice. Upon the closing of the Series B convertible preferred stock, the Company recorded a preferred stock tranche right liability of $4.6 million and a corresponding reduction to the carrying value of the Series B convertible preferred stock.

Concurrent with the original issuance of the Series B convertible preferred stock, six stockholders exercised their right to early exercise the Series B preferred stock tranche right and purchased 10,731,725 shares. Consequently, the Company recognized $1.2 million in additional paid-in capital associated with the simultaneous original issuance and early exercise. Additionally, the investors paid a premium of $1.7 million for these shares over their fair value which was also recorded in additional paid-in capital as a capital contribution.

Subsequent to the original issuance in August 2023, one stockholder exercised its right to early exercise the Series B preferred stock tranche right and purchased 4,769,655 shares of Series B convertible preferred stock for cash proceeds of $8.0 million. The fair value of the associated tranche right liability that was settled at the time of the sale of $0.5 million was recognized in additional paid-in capital. Additionally, the investor paid a premium of $0.8 million for these shares over their fair value which was also recorded in additional paid-in capital as a capital contribution.

As of December 31, 2023, the Company remeasured the Series B tranche right liability to be $4.2 million.

In February 2024, the Company's Series B convertible preferred stockholders voted to waive the second tranche milestones and purchase the remaining Series B Milestone Tranche shares. Immediately prior to the waiver, the Company remeasured the Series B tranche right liability to be $11.6 million and recognized $7.4 million in other expense for the change in the fair value of the Series B tranche right liability during the period. As a result of the waiver, the Company remeasured the Series B tranche right liability to be $4.2 million and recognized the change in fair value of $7.4 million in additional paid-in capital, as a capital contribution. In conjunction with the closing that occurred in March 2024, an aggregate of 38,157,240 shares of Series B convertible preferred stock were issued at a price of $1.67727 per share, resulting in total cash proceeds of $64.0 million, less $87 thousand of issuance costs. As a result of this issuance, the Series B preferred stock tranche right liability with a then fair value of $4.2 million was settled in full and recognized as part of the carrying value of the Series B convertible preferred stock.

Upon issuance of each series of Preferred Stock, the Company assessed the embedded conversion and liquidation features of the securities and determined that such features did not require the Company to separately account for these features.

Convertible preferred stock consisted of the following (in thousands, except share amounts):

	December 31, 2023					
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Conversion Price per share	Common Stock Issuable Upon Conversion
Series A convertible preferred stock	100,182,354	100,182,354	$ 89,487	$ 100,182	$ 8.5648	11,701,298
Series B convertible preferred stock	89,431,030	51,273,790	77,091	86,000	$ 14.3655	5,988,764
	189,613,384	151,456,144	$ 166,578	$ 186,182		17,690,062

In June 2024, all of the Company's outstanding shares of convertible preferred stock were converted into shares of common stock.

The holders of the convertible preferred stock had the following rights and preferences:

Voting

The holders of the convertible preferred stock were entitled to vote, together with the holders of common stock, as a single class, on all matters submitted to the shareholders for a vote and were entitled to the number of votes equal to the number of shares of common stock into which the convertible preferred stock could convert on the record date for determination of shareholders entitled to vote. A majority vote of the holders of convertible preferred stock along with a majority vote of the Series B convertible preferred stock (the "Required Vote") was required to, among others, liquidate or dissolve the Company, amend the certificate of incorporation or bylaws, reclassify common stock or establish another class of capital stock, create shares that would rank senior to or authorize additional shares of convertible preferred stock, declare a dividend or make a distribution, or change the authorized number of directors constituting the board of directors.

In addition, the holders of shares of Series A convertible preferred stock, voting exclusively and as a separate class, were entitled to elect up to three directors of the Company. The holders of shares of Series B convertible preferred stock, voting exclusively and as a separate class, were entitled to elect up to two directors of the Company.

Conversion

Each share of Series A convertible preferred stock was convertible into common stock, at any time, at the option of the holder, and without the payment of additional consideration, at the applicable conversion ratio then in effect, provided that such holder may waive such option to convert upon written notice to the Company. Holders of Series B convertible preferred stock were not entitled to elect to convert shares of Series B convertible preferred stock into shares of Common Stock at any time during the period commencing on the date of the first issuance of the Series B convertible preferred stock and ending immediately following the earliest to occur of (i) the Series B Milestone Tranche closing, (ii) the achievement of the second tranche milestone, (iii) the date such holder's obligation to purchase its Second Tranche Shares is fulfilled, (iv) the termination of such holder's obligations to complete the Series B Milestone Tranche closing and (v) such date as agreed to by the Company and the holders of a majority of the then outstanding shares of Series B convertible preferred stock, voting as a separate, exclusive class. In addition, each share of convertible preferred stock would be automatically converted into shares of common stock at the then-effective applicable conversion ratio upon either (i) the closing of a firm-commitment underwritten public offering of its common stock at a price per share of at least $14.70302 resulting in at least $50.0 million of gross proceeds, net of underwriting discount and commissions, to the Company, or (ii) the date specified by vote or written consent of the holders of the Required Vote, voting as a single class.

The conversion ratio of each class of convertible preferred stock was determined by dividing the Applicable Original Issue Price of each class of convertible preferred stock by the Conversion Price of each class. As of December 31, 2023, the Conversion Price was $8.5648 per share for Series A convertible preferred stock and $14.3655 per share for Series B convertible preferred stock, each subject to appropriate adjustment in the event of any share dividend, share split, combination or other similar recapitalization with respect to the convertible preferred stock. All outstanding convertible preferred stock was converted into common stock immediately prior to the closing of the Company's IPO.

There shall be no adjustment in the conversion price of the convertible preferred stock as the result of the issuance or deemed issuance of additional shares of the Company's common stock if the Company receives written notice from the holders of the Required Vote of the then outstanding shares of convertible preferred stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of additional shares of the Company's common stock.

In the event that any holder of convertible preferred stock who was required to participate in a subsequent closing pursuant to the purchase agreement did not purchase the aggregate number of subsequent closing shares, then each share of convertible preferred stock held by such holder shall automatically be converted into shares of common stock at a ratio of one share of common stock for every ten shares of convertible preferred stock held immediately prior to the consummation of such subsequent closing.

Dividends

The holders of the convertible preferred stock were entitled to receive, only when, as and if declared by the Board of Directors, non-cumulative dividends at the rate of 8% of the Applicable Original Issue Price of the convertible preferred stock (the "Preferred Dividend").

The Company shall not declare, pay or set aside any dividends on common shares of the Company unless the holders of convertible preferred stock then outstanding first received, or simultaneously received, the Preferred Dividend on each outstanding convertible preferred stock and a dividend on each outstanding convertible preferred stock in an amount at least equal to the product of (1) the dividend payable on each share of such class or series determined, as if all shares of such class or series had been converted into common stock and (2) the number of shares of common stock issuable upon conversion of a share of such series of convertible preferred stock, in each case calculated on the record date for determination of the holders entitled to receive such dividend. As of both December 31, 2024 and 2023, no cash dividends have been declared or paid.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, or upon the occurrence of a Deemed Liquidation Event (as defined below), the holders of shares of convertible preferred stock then outstanding were entitled, on a pari passu basis among the series of convertible preferred stock, to be paid out of the assets or funds of the Company available for distribution to stockholders before any payment was made to the holders of common stock. The holders of convertible preferred stock were entitled to an amount per share equal to the greater of (i) the Applicable Original Issue Price, plus any dividends declared but unpaid thereon, or (ii) the amount that would have been payable had all shares of each series of convertible preferred stock been converted into common stock immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event (as defined below). After the payment in full of the convertible preferred stock preference amount, the remaining assets of the Company available for distribution to stockholders shall be distributed among the holders of common stock on a pro rata basis.

Unless at least the holders of the Required Vote, elect otherwise, a Deemed Liquidation Event shall include a merger, consolidation, or share exchange (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company, or the closing of the transfer of 50% or more of the Company's outstanding voting stock, or any merger or consolidation in connection with a SPAC transaction or reverse merger transaction.

Redemption

The convertible preferred stock did not have redemption rights, except for the contingent redemption upon the occurrence of a Deemed Liquidation Event.

7. Common Stock

The voting, dividend and liquidation rights of the holders of the Company's common stock were subject to and qualified by the rights, powers and preferences of the holders of the convertible preferred stock set forth above. Each share of common stock entitles the holder to one vote, together with the holders of the convertible preferred stock, on all matters submitted to the stockholders for a vote. The holders of common stock are entitled to receive dividends, if any, as declared by the Company's board of directors, subject to the preferential dividend rights of convertible preferred stock. As of December 31, 2024 and 2023, no dividends have been declared or paid.

On May 30, 2024, the Company's stockholders approved the third amended and restated certificate of incorporation, which was filed upon the closing of the IPO on June 10, 2024 and which, among other things, increased the number of shares of common stock authorized for issuance from 250,000,000 to 500,000,000 shares of common stock.

In June 2024, the Company completed its IPO of its common stock. In connection with its IPO, the Company issued and sold 9,200,000 shares of its common stock at a price of $17.00 per share. As a result, the Company received $140.9 million in net proceeds, after deducting underwriting discounts and commissions and offering costs of $15.5 million.

In connection with its IPO, the Company issued and sold 1,058,824 shares of its common stock in a concurrent private placement, at a price of $17.00 per share, and received $16.7 million in net proceeds, after deducting placement agent fees and other private placement costs of $1.3 million.

As of December 31, 2023, the Company had reserved 23,890,096 shares of common stock, of which 22,146,816 were reserved for the potential conversion of shares of Series A convertible preferred stock and Series B convertible preferred stock, and 1,743,280 shares for issuance under the Company's 2022 Stock Option and Grant Plan, as amended (the "2022 Plan"). The Series A convertible preferred stock and Series B convertible preferred stock were converted to common stock immediately prior to completion of the IPO. As of December 31, 2024, the Company had reserved 6,852,229 shares of common stock, of which 2,713,368 shares were reserved for issuance under the 2022 Plan, 3,814,618 shares under the 2024 Stock Option and Grant Plan (the "2024 Plan") and 324,243 shares under the 2024 Employee Stock Purchase Plan (the "2024 ESPP") (see Note 8).

8. Stock-Based Compensation

2022 Plan

The 2022 Plan provides for the Company to grant incentive stock options ("ISO") or non-qualified stock options, unrestricted stock awards, restricted stock awards and restricted stock units (collectively, the "Awards") to the employees, directors, and consultants of the Company. The 2022 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or its committee if so delegated.

As of December 31, 2023, the total number of shares of common stock authorized and issuable under the 2022 Plan was 1,743,280. In March 2024, the Company's board of directors increased the number of shares of common stock reserved for issuance under the plan from 1,743,280 to 2,948,559 shares. The remaining shares reserved for issuance under the 2022 Plan ceased to be available for issuance at the time that the 2024 Plan became effective. There will be no further awards granted under the 2022 Plan, but all outstanding awards under the 2022 Plan will continue to be governed by their existing terms.

Subsequent to the effectiveness of the 2024 Plan, the shares of common stock underlying any awards under the 2022 Plan that are forfeited, canceled, reacquired by the Company prior to vesting, satisfied without the issuance of stock or otherwise terminated (other than by exercise) and shares withheld upon exercise of an option or settlement of an award to cover the exercise price or tax withholding will be added to the shares of common stock available for issuance under the 2024 Plan.

2024 Plan

In May 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 Plan, which became effective in June 2024. The 2024 Plan allows the Company to make equity-based and cash-based incentive awards to its officers, employees, directors, and consultants. The 2024 plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares initially reserved for issuance under the 2024 Plan is 3,814,618 shares. In addition, the number of shares reserved and

available for issuance under the 2024 Plan will automatically increase on January 1, 2025 and each January 1 thereafter, by five percent of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the compensation committee. As of December 31, 2024, the Company had 2,295,348 shares remaining available for future grants.

The shares of common stock underlying any awards under the 2024 Plan and the 2022 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of stock, expire, or are otherwise terminated (other than by exercise) will be added back to the shares of common stock available for issuance under the 2024 Plan.

2024 ESPP

In May 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 ESPP, which became effective in June 2024. The 2024 ESPP initially reserved and authorized the issuance of up to a total of 324,243 shares of the Company's common stock to participating employees. The 2024 ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2025 and each January 1 thereafter through January 1, 2034, by the lesser of (i) 648,486 shares of common stock, (ii) one percent of the outstanding number of shares of common stock on the immediately preceding December 31, or (iii) such lesser number of shares of common stock as determined by the administrator of the 2024 ESPP. The number of shares reserved under the 2024 ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

No shares were issued during the year ended December 31, 2024 relating to the 2024 ESPP.

Stock Option Valuation

The fair value of each stock option grant was estimated on the grant date using the Black-Scholes option-pricing model. The Company historically had been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

The following table presents the assumptions used in the Black-Scholes option-pricing model to determine the fair value of stock options granted:

	Year Ended December 31, 2024	Year Ended December 31, 2023
Expected volatility	83.80% - 99.30%	95.45% - 99.20%
Risk-free interest rate	3.55% - 4.48%	4.14% - 4.23%
Expected dividend yield	0.00%	0.00%
Expected term (in years)	5.85 - 6.08	4.0 - 6.0
Fair value of common stock	$6.34 - $26.90	$ 0.74

Stock Options

The Company has granted stock options with service-based vesting conditions. Stock options generally vest over four years and have a maximum term of ten years. Prior to the IPO, the Company typically granted stock options to employees and non-employees at exercise prices deemed by the Board to be equal to the fair value of the common stock at the time of grant. Subsequent to the IPO, exercise prices are determined by the closing price of the Company's stock on the date of the grant. The following table summarizes the Company's stock option activity for the year ended December 31, 2024:

	Number of Shares	Weighted-Average Exercise Price per share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2023	1,376,596	$ 1.80	9.83	$ 6,249
Granted	2,869,503	13.95		
Exercised	(3,745)	1.80		
Forfeited	(52,608)	9.94		
Expired	—	—		
Options outstanding at December 31, 2024	4,189,746	$ 10.02	9.19	$ 34,324
Options vested and exercisable at December 31, 2024	465,541	2.13	8.62	7,268
Options vested and expected to vest at December 31, 2024	4,189,746	$ 10.02	9.19	$ 34,324

The weighted-average grant-date fair value of stock options granted during the years ended December 31, 2024 and 2023 was $11.35 per share and $5.74 per share, respectively. As of December 31, 2024, there was $32.5 million of total unrecognized compensation cost related to unvested stock options, which is expected to be recognized over a remaining weighted average period of 3.1 years.

Restricted Stock Awards ("RSA")

The Company has awarded restricted stock both under the 2022 Plan as well as outside of the 2022 Plan.

Service-Based RSAs

The majority of the RSAs have service-based vesting conditions and vest over a period from immediately to four years. Compensation expense is recognized on a straight-line basis over the requisite service period.

The following table summarizes the Company's service-based RSA grant activity for the year ended December 31, 2024:

	RSAs	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	1,585,998	$ 3.64
Granted	—	—
Vested	(609,402)	3.70
Forfeited	—	—
Unvested shares at December 31, 2024	976,596	$ 3.69

The aggregate intrinsic fair value of service-based RSAs that vested during the years ended December 31, 2024 and 2023, was $10.1 million and $2.2 million, respectively. The aggregate intrinsic value of restricted stock awards is calculated as the positive difference between the prices paid, if any, of the restricted stock awards and the fair value of the Company's common stock.

As of December 31, 2024, there was $3.5 million of total unrecognized compensation cost related to unvested service-based RSAs, which is expected to be recognized over a remaining weighted average period of 2.0 years.

Performance-Based RSAs

The Company has also granted performance-based RSAs to certain employees and directors with a vesting commencement date contingent upon the subsequent closing of the Company's Series A convertible preferred stock financing. The Company has determined that it has met all the conditions to establish the grant date for these performance-based RSAs at the original issuance date. Therefore, these awards are deemed to contain an implied performance condition. The vesting of the performance-based RSAs is also subject to grantees' continued service until the 4th anniversary date of the closing of a subsequent financing.

Share-based compensation expense associated with the performance-based RSAs is recognized if the performance condition is considered probable of achievement. In February 2023, the existing Series A convertible preferred stock investors waived the second and third tranche milestones and the Company closed on the sale of its second and third tranches of Series A convertible preferred stock. As a result, the performance condition was deemed to be met.

The following table summarizes the Company's performance-based RSA grant activity for the year ended December 31, 2024:

	RSAs	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	649,264	$ 3.63
Granted	—	—
Vested	(205,029)	3.63
Forfeited	—	—
Unvested shares at December 31, 2024	444,235	$ 3.63

The aggregate intrinsic fair value of performance-based RSAs that vested during the years ended December 31, 2024 and 2023 was $3.4 million and $0.8 million, respectively. The aggregate intrinsic value of restricted stock awards is calculated as the positive difference between the prices paid, if any, of the restricted stock awards and the fair value of the Company's common stock.

As of December 31, 2024, there was $0.5 million of total unrecognized compensation cost related to unvested performance-based restricted common stock, which is expected to be recognized over a remaining weighted average period of 1.36 years.

Performance-Based Restricted Stock Units ("PSUs")

In December 2024, the Company granted 95,500 performance-based restricted stock units ("PSUs") to certain employees. Each PSU represents a right to receive one share of the Company's Common Stock when it becomes vested. The PSUs will vest in two equal tranches over two performance periods starting on the grant date and ending, respectively, on December 31, 2025, and December 31, 2026, subject to the satisfaction of both service and performance conditions specifically defined for each performance period and each PSU award. The performance conditions are related to the achievement of certain program milestones in the Company's drug discovery and development process. As of December 31, 2024, the Company has not recognized any compensation expenses for the PSUs because none of the performance conditions were considered probable of being met.

The grant-date fair value of the PSU is $21.56. As of December 31, 2024, the unrecognized compensation expenses associated with the PSUs were $2.1 million.

Stock-Based Compensation

The Company recorded stock-based compensation expense for stock options of $7.4 million and $0.2 million in the years ended December 31, 2024 and 2023, respectively. The Company recorded stock-based compensation expense for RSAs of $2.8 million and $3.3 million in the years ended December 31, 2024 and 2023, respectively. The following table below summarizes the classification of the Company's stock-based compensation expense related to stock options and restricted common stock awards in the consolidated statements of operations and comprehensive loss (in thousands):

	For the year ended December 31, 2024	2023
General and Administrative	$ 6,190	$ 1,637
Research and Development	4,045	1,888
	$ 10,235	$ 3,525

9. Leases

Operating Lease

In June 2023, the Company entered into a lease for its corporate headquarters in Boston, Massachusetts. The lease commenced August 31, 2023 with an initial term of 40 months. The monthly lease payments are $66 thousand for the first 12 months, with 2% escalation each year. In conjunction with the lease, the Company paid a security deposit of $0.1 million that is recorded on the Company's consolidated balance sheet in other assets as of December 31, 2024.

Right-of-use lease assets and lease liabilities are reported in the Company's consolidated balance sheets as follows (in thousands):

	For the year ended December 31,	
	2024	**2023**
Operating lease		
Operating lease right-of-use assets, net	$ 1,442	$ 2,084
Operating lease right-of-use liabilities, current	737	670
Operating lease right-of-use liabilities, non-current	739	1,476
Total operating lease liabilities	$ 1,476	$ 2,146

The components of operating lease costs were as follows (in thousands):

	For the year ended December 31,	
	2024	**2023**
Operating lease costs	$ 776	$ 261
Variable lease costs	383	9
Short-term lease costs	66	382
Total Lease cost	$ 1,225	$ 652

Other information related to leases was as follows (in thousands):

Supplemental cash flow information

	For the year ended December 31, 2024	2023
Cash flows included in the measurement of lease liabilities:		
Cash paid for amounts included in the measurement of operating lease liabilities	$ 804	$ 199
Right-of-use lease assets obtained in exchange for new operating lease liabilities	$ —	$ 2,290

Lease term and discount rate

	December 31, 2024	2023
Weighted-average remaining lease term–operating lease	2	3
Weighted-average discount rate–operating lease	7.29%	7.29%

In February 2024, the Company entered into a lease for laboratory and office space in San Diego, California with a lease term of 5 years for which the Company expects to pay $9.6 million over the lease term. Per the terms of the lease, the landlord will deliver the space to the Company on the lease commencement date, which is no earlier than November 2024. As of December 31, 2024, the Company has not yet occupied the lease space and therefore, the Company has not recorded a corresponding right-of-use asset or liability on the consolidated balance sheet as of December 31, 2024.

In November 2024, the Company entered into a sublease for office space in Boston, Massachusetts with a lease term of 6.5 years for which the Company expects to pay $5.2 million over the sublease term. Per the terms of the sublease, the landlord will deliver the space to the Company on the sublease commencement date, which is anticipated to be June 1, 2025. As of December 31, 2024, the Company has not yet occupied the lease space and therefore, the Company has not recorded a corresponding right-of-use asset or liability on the consolidated balance sheet as of December 31, 2024.

As of December 31, 2024, maturities of operating lease liabilities for each of the following five years and a total thereafter were as follows (in thousands):

2025	$ 820
2026	766
Total minimum future lease payments	$ 1,586
Less: Imputed interest	(110)
Total lease liabilities	$ 1,476

10. Related Party Transactions

Janssen

Janssen Pharmaceutical NV ("Janssen") is a related party to a founding investor in the Company, Johnson & Johnson Innovation—JJDC, Inc., as both entities are direct subsidiaries of Johnson & Johnson, Inc. For the years ended December 31, 2024 and 2023, the Company incurred costs of $69 thousand and $0.4 million, respectively, which was recognized as research and development expense in the consolidated statement of operations and comprehensive loss, to Janssen for the use of lab space in California. As of December 31, 2024 and 2023, there were no related party transactions in accounts payable or accrued expenses.

Third Rock Ventures

Third Rock Ventures LLC ("Third Rock") is a founding investor in the Company. For the years ended December 31, 2024 and 2023, the Company incurred costs of $0.1 million and $1.2 million, respectively, of which zero and $0.3 million, respectively, was recognized as research and development expense, and $0.1 million and $0.9 million, respectively, was recognized as general and administrative expense in the consolidated statement of operations and comprehensive loss to Third Rock primarily for management consulting and other various start-up support activities. As of December 31, 2024 and 2023, zero and $0.2 million, respectively, was included in accounts payable. As of both December 31, 2024 and 2023, there were no accrued expenses related to Third Rock.

11. Segment

The Company is currently developing medicines for patients with neurological or psychiatric disorders in the United States. The Company does not have any revenue generating products, and revenue will not be generated from any other current or future product candidates until regulatory approval is obtained and products are commercialized.

For the year ended December 31, 2024, the Company has identified one operating and reportable segment. The Company defines its operating segments based on internally reported financial information that is regularly reviewed by the Chief Operating Decision Maker ("CODM") to analyze financial performance, make decisions, and allocate resources. The Company's Chief Executive Officer ("CEO") is the CODM.

The CODM reviews the segment's profit or loss based on net (loss) income reported on the consolidated statement of operations and comprehensive (loss) income and considers forecast-to-actuals variances on a quarterly basis for expenses that are deemed significant. Further, the CODM reviews the segment's assets based on total assets reported on the consolidated balance sheet. All long-lived assets are held in the United States.

The Company's CODM views specific categories within research and development expenses and general and administrative expenses as significant given the direct correlation between cash burn and profitability as a pre-revenue company. The following table reconciles reported revenues to net (loss) income under the significant expense principle for the years ended December 31, 2024 and 2023 (in thousands):

	For the year ended December 31,	
	2024	2023
Research and Development Expenses:		
RAP-219 program external expenses	$ 22,080	$ 10,202
Preclinical programs external expenses	16,535	6,335
R&D personnel-related costs (including stock-based compensation)	19,500	9,939
Other costs	2,820	1,523
General and Administrative Expenses:		
G&A personnel-related costs (including stock-based compensation)	13,989	4,324
Professional and consulting costs	5,482	3,158
Facility related and other	2,649	698
Loss from operations	$ (83,055)	$ (36,179)
Interest income	12,138	2,527
Change in fair value of preferred stock tranche right liability	(7,390)	(1,124)
Net loss before income taxes	(78,307)	(34,776)
Provision for income taxes	—	10
Net loss	$ (78,307)	$ (34,786)

Accordingly, the Company consists of a single operating and reportable segment and the consolidated financial statements and notes thereto are presented as a single reportable segment.

12. Income Taxes

For the years ended December 31, 2024 and 2023, the Company recorded a tax provision of zero and $10 thousand, respectively. In addition, the Company has recorded a full valuation allowance against its net deferred tax assets as of December 31, 2024 and 2023.

The components of income tax provision are as follows (in thousands):

	For the year ended December 31,	
	2024	2023
Components of income tax provision		
Current Provision:		
Federal	$ —	$ —
State	—	10
Total current provision	—	10
Deferred income tax provision (benefit)	—	—
Federal	—	—
State	—	—
Total deferred income tax provision (benefit)	—	—
Total provision for (benefit from) income taxes	$ —	$ 10

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	For the year ended December 31,	
	2024	2023
Rate Reconciliation		
Statutory U.S. federal rate	21.00%	21.00%
Permanent Differences	-3.59%	-0.84%
State income taxes, net of federal benefit	2.44%	6.47%
Research and development credits	3.62%	3.64%
Other	-1.68%	0.00%
Valuation allowance	-21.79%	-30.30%
Effective tax rate	0.00%	-0.03%

The Company accounts for income taxes in accordance with ASC Topic 740. Deferred income tax assets and liabilities are determined based upon temporary differences between the 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.

Net deferred tax assets (liabilities) consisted of the following (in thousands):

	As of December 31,	
	2024	2023
Deferred Tax Summary		
Deferred tax assets:		
US and State net operating loss carryforwards	$ 3,246	$ 1,345
Capitalized research and development costs	19,043	7,307
Depreciation	—	—
License fees capitalization	1,022	1,211
Stock-based compensation	1,049	1,041
Research and development credit carryforwards	5,065	1,837
Lease liability	355	567
Accruals and other	853	635
Total deferred tax assets	30,633	13,943
Deferred tax liabilities		
Depreciation	(75)	(27)
Right-of-Use Asset	(347)	(551)
481(a) Adjustment	—	(220)
Total deferred tax liabilities	(422)	(798)
Valuation Allowance	(30,211)	(13,145)
Net deferred tax assets (liabilities)	$ —	$ —

For the years ended December 31, 2024 and 2023, the Company had U.S. federal net operating loss carryforwards of $13.7 million and $6.0 million and state net operating loss carryforwards of $12.0 million and $1.6 million, respectively. Federal losses have an indefinite carryforward period, but can only offset 80% of federal taxable income in a given year. Losses for state purposes begin to expire in 2043. For the years ended December 31, 2024 and 2023, the Company had federal research and development tax credit carryforwards of $3.8 million and $1.5 million, and state research and development tax credit carryforwards of $1.6 million and $0.5 million, respectively, which begin to expire in 2042 and 2037.

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of amortizable license fees, capitalized research and development expenses, and net operating loss carryforwards. Under the applicable accounting standards, management has considered the Company's activity and concluded that it is more likely than not that the Company will not recognize the benefits of domestic deferred tax assets. Accordingly, a full valuation allowance of $30.2 million as of December 31, 2024 and $13.1 million as of December 31, 2023, respectively, was recorded. Changes in valuation allowance for deferred tax assets for the years ended December 31, 2024 and 2023 related primarily to the increases in NOLs, research and development tax credit carryforwards, capitalized research and development expenses pursuant to IRC Section 174, and stock-based compensation were as follows:

	For the year ended December 31,	
	2024	2023
Valuation allowance as of beginning of year	$ (13,145)	$ (2,609)
Decreases recorded as benefit to income tax provision	—	—
Increases recorded to income tax provision	(17,066)	(10,536)
Valuation allowance as of end of year	$ (30,211)	$ (13,145)

The federal and state net operating loss and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, and similar state provisions, due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. As of December 31, 2024, the Company has not completed a 382 study to assess whether a change of ownership has occurred since its formation.

Section 174 made by the Tax Cuts and Jobs Act of 2017 (the TCJA) for tax year beginning on or after Jan. 1, 2022, no longer permits an immediate deduction for research and development expenditures in the tax year that such costs are incurred. Section 174 costs are expenditures which represent research and development costs that are incident to the development or improvement of a product, process, formula, invention, computer software or technique. The research and experimental ("R&E") expenses under

Section 174 must be capitalized and amortized over five years for research performed in the U.S. and 15 years for research performed outside the U.S. We have included the impact of this provision, which results in a deferred tax asset of approximately $19.0 million as of December 31, 2024 and $7.3 million as of December 31, 2023.

The Company adopted the authoritative guidance on accounting for and disclosure of uncertain tax positions, which requires the Company to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority. As of December 31, 2024, the Company had not recorded any reserves for uncertain tax positions or related interest and penalties. The Company's policy is to record interest and penalties related to income taxes as part of the tax provision.

The Company files income tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions in the United States and other countries, where applicable. There are currently no pending tax examinations. The Company is open to federal and state tax examination under statute from 2022 to present. Carryforward attributes from prior years can be adjusted upon examination by federal and state tax authorities to the extent utilized in an open tax year or in future periods.

There are no tax matters under discussion with taxing authorities that are expected to have a material effect on the Company's consolidated financial statements.

13. Commitments and Contingencies

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scopes and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with the board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any indemnification arrangements that could have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2024 and 2023.

Legal Proceedings

From time to time, the Company may become involved in legal proceedings or other litigation relating to claims arising in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated. Significant judgment is required to determine both probability and estimated exposure amount. Legal fees and other costs associated with such proceedings are expensed as incurred. As of December 31, 2024 and 2023, the Company was not a party to any material legal proceedings or claims.

NeuroPace Master Services Agreement and Statement of Work

In November 2023, the Company entered into a master services agreement (the "NeuroPace Agreement") with NeuroPace Inc. ("NeuroPace"), the manufacturer and distributor of the RNS system. Pursuant to the NeuroPace Agreement and in accordance with statement of work agreements entered into from time to time, NeuroPace provides the Company with certain services with respect to data from the RNS systems used in our clinical trials. The NeuroPace Agreement also grants the Company a royalty-free, worldwide, exclusive, non-transferable license to all data collected by the RNS systems in its Phase 2a clinical trial and the outcomes of algorithms that are applied to such data, as well as the ability to publish the outcomes of algorithms, subject to certain conditions. The consideration the Company will pay to NeuroPace for such services is set out in each statement of work agreement.

The NeuroPace Agreement contains an exclusivity provision providing that, at any time while providing services under the NeuroPace Agreement and for a period after the final clinical study report, NeuroPace may not perform any services that are the

same as the services covered by the NeuroPace Agreement to any business that directly competes with us, subject to the specific terms of the NeuroPace Agreement. The NeuroPace Agreement also contains standard representations and warranties, confidentiality and intellectual property protective provisions and indemnification terms.

The NeuroPace Agreement expires on the later of three years from the effective date or the completion of all services under all statement of work agreements entered into prior to the third anniversary of the effective date. Either party may terminate the NeuroPace Agreement or any statement of work agreement (i) without cause by giving written notice to the other party within a specified period of time, (ii) by giving written notice upon a curable material breach that is not remediated within a specified period of time, or (iii) immediately upon written notice in the event of a material breach that cannot be cured.

Concurrently with the execution of the NeuroPace Agreement, the parties also entered into an initial statement of work under the NeuroPace Agreement, as amended in March 2024 (the "NeuroPace SOW"), pursuant to which NeuroPace agreed to provide services related to the Company's Phase 2a clinical trial of RAP-219, including, among other things, clinical trial readiness support, identification of potential patients satisfying the enrollment criteria and RNS system data reporting and data analysis. Pursuant to the payment schedule set out in the NeuroPace SOW, we will pay NeuroPace an aggregate of up to $3.7 million over a period of approximately two years in connection with NeuroPace's provision of services and achievement of certain patient enrollment and deliverable milestones. During the year ended December 31, 2024, the Company paid NeuroPace $0.6 million and recognized $1.8 million in research and development expense for services performed, resulting in a prepaid expense balance of $0.3 million as of December 31, 2024. As of December 31, 2023, $1.5 million was recorded as prepaid expenses and other current assets in the consolidated balance sheet.

14. Net Loss per Share

Basic and diluted net loss per common share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2024	2023
Numerator:		
Net loss attributable to common stockholders	$ (78,307)	$ (34,786)
Denominator:		
Weighted average common shares outstanding, basic and diluted	20,738,338	1,505,774
Net loss per share attributable to common stockholders, basic and diluted	$ (3.78)	$ (23.10)

For purposes of this calculation, the Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share available to common shareholders for the periods indicated because including them would have had an anti-dilutive effect:

	As of December 31,	
	2024	2023
Series A convertible preferred stock	—	11,701,298
Series B convertible preferred stock	—	5,988,764
Options to purchase common stock	4,189,746	1,376,596
Unvested restricted common stock—service based	976,596	1,585,998
Unvested restricted common stock—performance based	444,235	649,264
Total	5,610,577	21,301,920

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

None.

Item 9A. Controls and Procedures.

Management's Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed by us in the reports we file or submit under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the U.S. Securities and Exchange Commission ("SEC"). Our disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating the disclosure controls and procedures, our 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. As required by Rule 13a-15(b) or Rule 15d-15(b) promulgated by the SEC under the Exchange Act, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K (this "Annual Report"). Based on the foregoing, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Annual Report at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies. Additionally, our independent registered public accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the Jumpstart Our Business Startups Act.

Changes in Internal Control over Financial Reporting

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

Item 9B. Other Information.

(a) None.

(b) During the quarter ended December 31, 2024, the following directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) adopted certain trading plans intended to satisfy the requirements of Rule 10b5-1(c):

Name *(Title)*	Action Taken *(Date of Action)*	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Cheryl Gault (*Chief Operating Officer*)	Adoption (*December 11, 2024*)	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c)	Sale of the Company's common stock pursuant to the terms of the plan	Approximately 8 months	10,000

Abraham Ceesay *(Chief Executive Officer)*	Adoption *(December 12, 2024)*	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c)	Sale of the Company's common stock pursuant to the terms of the plan	Approximately 11 months	131,000 [(1)]
David Bredt *(Chief Scientific Officer)*	Adoption *(December 12, 2024)*	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c)	Sale of the Company's common stock pursuant to the terms of the plan	Approximately 11 months	102,000

(1) Consists of 70,000 shares held by Mr. Ceesay and 61,000 shares held by The Dorothy Ceesay Irrevocable Trust.

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 10 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission 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 12 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

Financial Statements

For a list of the financial statements included herein, see the Index to Consolidated Financial Statements under Item 8 of this Annual Report on Form 10-K, which is incorporated by reference.

Financial Statement Schedules

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

Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K:

Exhibit Number	Description
3.1	Third Amended and Restated Certificate of Incorporation of Rapport Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on June 10, 2024).
3.2	Amended and Restated Bylaws of Rapport Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed on June 10, 2024).
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
4.2	Amended and Restated Investors' Rights Agreement, by and among the Company and certain of its stockholders, dated as of August 7, 2023 (incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
4.3*	Description of Securities of the Company.
10.1#	Form of Stock Purchase Agreement, by and among the Company and the Purchasers party thereto (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on June 10, 2024).
10.2#	Rapport Therapeutics, Inc. 2024 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 to Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on June 3, 2024).
10.3#	2024 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on June 3, 2024).
10.4#	Indemnification Agreement (incorporated by reference to Exhibit 10.4 to Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on June 3, 2024).
10.5#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.5 to Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on June 3, 2024).
10.6#	Rapport Therapeutics, Inc. Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.6 to Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on June 3, 2024).
10.7#	Employment Agreement, by and between the Company and Abraham N. Ceesay, M.B.A., effective as of June 10, 2024 (incorporated by reference to Exhibit 10.7 to the Company's Form 10-Q filed on August 8, 2024).
10.8#	Employment Agreement, by and between the Company and Troy Ignelzi, effective as of June 10, 2024(incorporated by reference to Exhibit 10.8 to the Company's Form 10-Q filed on August 8, 2024).
10.9†+	Employment Agreement, by and between the Company and Cheryl Gault, effective as of June 10, 2024 (incorporated by reference to Exhibit 10.9 to the Company's Form 10-Q filed on August 8, 2024).
10.10†+	Option and License Agreement, by and between the Company and Janssen Pharmaceutica NV, dated August 9, 2022, as amended (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
10.11†+	Master Services Agreement, by and between the Company and NeuroPace Inc., dated November 28, 2023. (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
10.12†+	Statement of Work #1, by and between the Company and NeuroPace Inc., dated November 28, 2023, as amended March 1, 2024 (incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).

10.13†+	Sublease Agreement, by and between the Company and Whoop, Inc., dated June 15, 2023 (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
10.14†+	Lease Agreement, by and between the Company and ARE-9880 Campus Point, LLC, dated February 12, 2024 (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
19.1*	Rapport Therapeutics, Inc. Insider Trading Policy.
21.1	Subsidiaries of the Company (incorporated by reference to Exhibit 21.1 to the Company's Registration Statement on Form S-1 filed on May 17, 2024).
23.1*	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1*	Rapport Therapeutics, Inc. Compensation Recovery Policy.
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents.
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document and included in Exhibit 101).

* Filed herewith.
** Furnished herewith.
# Indicates a management contract or any compensatory plan, contract or arrangement.
† Certain portions of this document that constitute confidential information have been redacted pursuant to Item 601(b)(10) of Regulation S-K.
+ Certain exhibits and schedules to these agreements have been omitted pursuant to Item 601(a)(5) and (6) of Regulation S-K. The Company will furnish copies of any of the exhibits and schedules to the Securities and Exchange Commission upon request.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Rapport Therapeutics, Inc.

Date: March 11, 2025

By: /s/ Abraham N. Ceesay
Abraham N. Ceesay, M.B.A.
Chief Executive Officer and Director

POWER OF ATTORNEY AND SIGNATURES

KNOW ALL BY THESE PRESENT, that each individual whose signature appears below hereby constitutes and appoints each of Abraham N. Ceesay, M.B.A. and Troy Ignelzi, as such person's true and lawful attorney-in-fact and agent with full power of substitution and resubstitution, for such person in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Annual Report on Form 10-K has been signed by the following person in the capacities and on the date indicated.

Signature	Title	Date
/s/ Abraham N. Ceesay Abraham N. Ceesay, M.B.A.	Chief Executive Officer and Director (*Principal Executive Officer*)	March 11, 2025
/s/ Troy Ignelzi Troy Ignelzi	Chief Financial Officer (*Principal Financial Officer and Principal Accounting Officer*)	March 11, 2025
/s/ Steven M. Paul Steven M. Paul, M.D.	Director and Chairman	March 11, 2025
/s/ James I. Healy James I. Healy, M.D., Ph.D.	Director	March 11, 2025
/s/ John Maraganore John Maraganore, Ph.D.	Director	March 11, 2025
/s/ Paul Silva Paul Silva	Director	March 11, 2025
/s/ Raymond Sanchez Raymond Sanchez, M.D.	Director	March 11, 2025
/s/ Robert J. Perez Robert J. Perez	Director	March 11, 2025
/s/ Reid Huber Reid Huber, Ph.D.	Director	March 11, 2025
/s/ Wendy B. Young Wendy B. Young, Ph.D.	Director	March 11, 2025